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ANNALS
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XXI

THE NATURE OF COCHLEAR ACTIVITY AFTER DEATH

ERNEST GLEN WEVER, Ph.D.
CHARLES W. BRAY, Ph.D.
AND
MERLE LAWRENCE, Ph.D.

PRINCETON, N. J.

A number of investigators have observed the deterioration of the electrical responses of the ear after death of the animal. In early studies of these responses the changes that follow death were of special interest as indicative of the physiological character of the phenomena.[1] The deterioration occurs for all forms of auditory potentials: those from the cochlea, the auditory nerve, and higher acoustic tracts. However, the rate of deterioration varies according to the source of the potentials. It is most rapid for impulses from the central tracts, and least rapid for the cochlear responses.

Most observers have reported that the nervous effects drop abruptly at the moment of cardiac failure, and soon thereafter cease to be detectable. The cochlear responses, on the other hand, remain for a considerable time. The times reported for the cochlear potentials vary among different observers from a few minutes to an hour or more after death. These differences no doubt arise from variations in experimental procedures and in the sensitivity of recording apparatus.

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Curves representing the death function have been given in only two reports. Davis and others[1] gave curves for two cats which showed the magnitude of the cochlear responses during 50 minutes after death. Hallpike and Rawdon-Smith[2] presented such curves for one cat over a period of 15 minutes. In the latter experiment two different tones were used as test stimuli, and a similar course of decline was observed for each. The conclusion was reached that the changes after death were not significantly related to tonal frequency.

The present investigation is concerned with the death function for the cochlear response. The phenomenon is considered with respect to the cause of death, the conditions of stimulation, and the concomitant physiological changes. The experiments were carried out on 16 guinea pigs and four cats.

PROCEDURE

The potentials were picked up by a silver foil electrode on the round window membrane, and after amplification were measured either with a cathode ray oscillograph or a wave analyzer (General Radio Type 736 A) used as a selective voltmeter. The stimuli were pure tones from a loudspeaker. Calibrations of both stimulating and recording apparatus make it possible to report all data in absolute terms.

Measurements were made on the living animal over a sufficient period to indicate the normal condition, and then the animal was killed by one of four methods as described below. Readings were resumed as soon as possible after the killing procedure, and continued for periods which varied in different experiments from 30 minutes to more than five hours.

RESULTS

Effect of the form of death.—Four procedures were used to produce death. They were (1) pithing the medulla (six animals), (2) clamping the heart (three animals), (3) clamping the trachea (seven animals), and (4) poisoning with curare (four animals). All these operations were carried out under deep Urethane anesthesia. The procedures show differences in the rate of the death process, in the amount of activity caused, and in the effects upon the cochlear responses.

(1) Pithing the medulla.—Death, as diagnosed by the usual signs of cessation of respiratory and cardiac movements, is most prompt after pithing the medulla. As the operation is carried out there is general, violent activity due to the stimulation of motor

centers, but in a few seconds all movement ceases. The blood vessels to the cochlea are severed in this operation.

Immediately after death the cochlear responses show an abrupt drop and then a more gradual decline which lasts for a considerable time. Figure 1 shows results for one of the animals. Tests were carried out with a tone of 1000~ presented at frequent intervals at an intensity sufficient to produce a response of about 100 microvolts under normal conditions. The medulla was pithed at the time indicated at *a* on the graph. As the curve shows, the response fell 12 db. during the first five minutes, and then leveled out somewhat to a gradual decline that lasted for more than an hour, when the observations ended. The curve shows many irregularities. The slight rise near the end of the abrupt drop is a characteristic feature.

(2) Clamping the heart.—In the procedure for clamping the heart, the thorax is first opened, whereupon the lungs collapse. Anoxemia therefore sets in before clamping the heart vessels is actually effected, and the early loss of responses is due in part to this change. After the clamping there is considerable and prolonged activity.

Figure 2 presents results with this procedure, with 300~ as the test tone. The time of opening the thorax is indicated by *a*, and the time of clamping the heart by *b*. The cochlear responses dropped rapidly during the first three or four minutes, much as described for the previous procedure, but at the end of this period the leveling off was much less. The rapid decline continued almost to the end of the period of observation, about 40 minutes after clamping, by which time the total loss of responses amounted to about 25 db.

(3 Clamping the trachea.—The activity caused by clamping the trachea is more prolonged but less violent than that for the two procedures just described. Convulsive respiratory movements and heart contractions continue for several minutes.

Figure 3 shows results in an animal that was tested with a tone of 1000~ at intervals of 20 seconds for five hours. In this experiment the vagus nerves were cut to eliminate central inhibitory impulses to the heart. At the time indicated at *a* the right vagus nerve was tied, at *b* the left vagus was tied, and at *c* and *d* these nerves were severed. The trachea was clamped at *e*, and the heart beat could no longer be detected by stethoscope at *f*.

The curve shows a slight drop immediately following the tying of the right vagus nerve, due probably to respiratory disturbance, but the further manipulations had little effect. Within about two

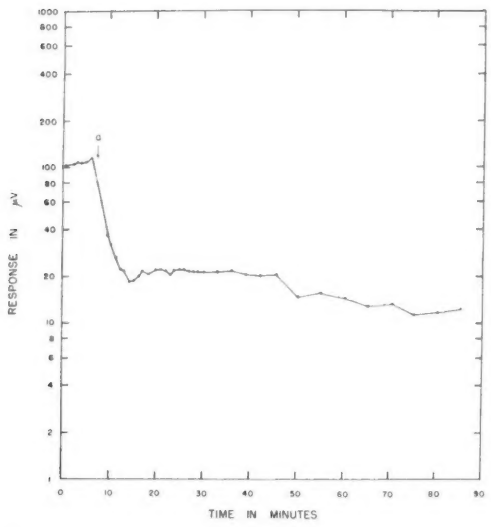

Fig. 1. Effect of death by pithing the medulla. Test tone, 1000~. The arrow at *a* shows the time of pithing. Guinea pig No. 162.

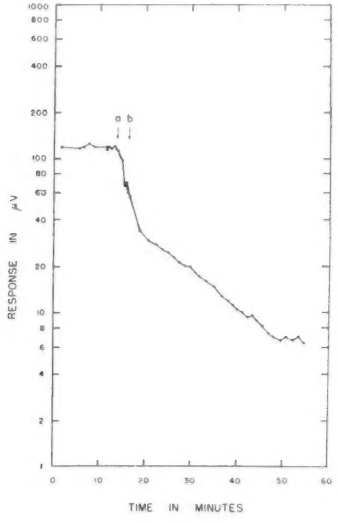

Fig. 2. Effect of death by clamping the heart. Test tone, 300~. Thorax opened at *a*, and heart clamped at *b*. Guinea pig No. 247.

minutes after clamping the trachea the responses began a rapid drop that lasted for four minutes, and then gave way to a limited rise. This rise ended as the heart ceased, and was followed by a secondary decline of moderate rate. After about 90 minutes a secondary rise began, which continued for about 40 minutes. Thereafter the responses decreased rather steadily for over two hours, when observations ceased.

(4) Curare poisoning.—The fourth procedure consisted of the administration of a lethal dose of curare. Results are shown in Fig. 4. The dose was given in three injections, indicated at *a*, *b* and *c*. At *d* respiration stopped, and at *e* the heart beat could no longer be detected.

The cochlear responses were tested at intervals of 20 seconds with a tone of 1000~. During the preliminary course of the experiment the responses were uniform, but began to decline rapidly about one minute before the heart stopped. This decline lasted for four minutes, and gave way to a period of stability that lasted about two minutes. After a further moderate decline a second period of leveling off appeared, and then a slight rise, about 30 minutes after death. This rise was followed by a slow and limited decline and a long period of stability and finally, about two and a half hours after death, by a second rise. Two further undulations complete the course for the period of observation.

The results of the four procedures may now be compared. All produce a rapid initial loss of responses, but differences appear in the amount and rate of this loss. For the first three procedures the initial loss is of the order of 15 to 20 db., while for curare poisoning it is usually about 10 db. The rate of decline is particularly rapid after clamping the heart.

The later course of the death function is complex, and variations among animals make difficult the comparison of different procedures. Generally, however, clamping the heart gives the most persistent decline, pithing the medulla and clamping the trachea give somewhat smaller changes, while curare produces the most moderate effects. These differences seem to be related to the amount of convulsive movements in the process of dying, and probably are due to injuries caused by pressure changes in the cochlea. Agonal changes in the cochlea are frequently observed in human and animal ears prepared for histological study.

The variations in rate of decline, and especially the phases of partial recovery, are curious features. Our attempts to account for

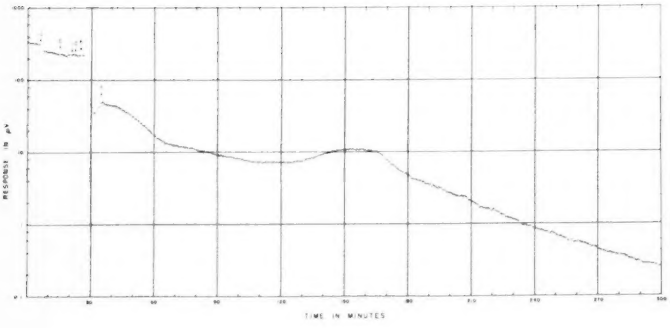

Fig. 3. Effect of death by clamping the trachea. Test tone, 1000~. At *a* to *d* vagus nerves tied and severed, at *e* trachea clamped, and at *f* heart stopped. Guinea pig No. 248.

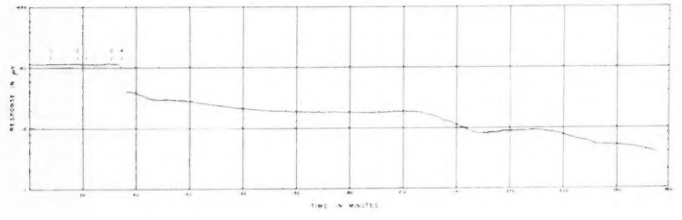

Fig. 4. Effect of death by curare poisoning. Test tone, 1000~. Curare administered at *a*, *b*, and *c*. Respiration ceased at *d*, and heart stopped at *e*. Guinea pig No. 261 L.

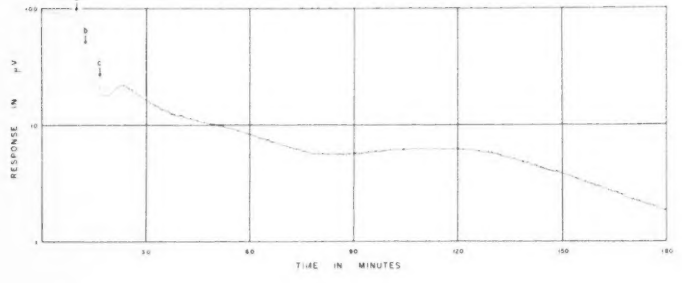

Fig. 5. The death function after destruction of the middle ear. Test tone, 1000~, presented by bone conduction. Trachea clamped at *a*, respiration ceased at *b*, and heart stopped at *c*. Guinea pig No. 266.

these variations have been successful mainly to the extent of eliminating certain possibilities.

The first recovery phase.—The first explanation considered for the "rebound" that follows the initial drop, as shown in Fig. 3, was that it resulted from relaxation of the tympanic muscles. It appeared likely that in the death process proper, when there is much mass activity, the tympanic muscles would be involved, and their contractions would add to the reduction of responses. As the death process enters its final stage, with muscular impairment through anoxemia, it is expected that the middle ear muscles would relax and permit greater transmission of sounds to the cochlea.

This hypothesis was tested by experiments in which the middle ear was destroyed and stimuli were applied by bone conduction. Results of one of these experiments are shown in Fig. 5, with 1000~ as the test tone. The early measurements were made after the middle ear operation, and the animal was then killed by clamping the trachea at the time indicated by *a*. At *b* respiration ceased and at *c* the heart stopped. The responses fell rapidly for six minutes and then rose, much as in the other experiments in which the middle ear was intact. It is evident that the middle ear is not responsible for the first recovery phase.

Late recovery phases.—Obviously, no active role can be presumed for the tympanic muscles an hour or more after death, but it is conceivable that at such times coagulatory or other changes might alter their tension. However, the results just presented do not support such a conception. In Fig. 5 a definite recovery phase is indicated 85 to 115 minutes after death, in an animal without the middle ear mechanism.

Relation to blood pressure.—Cats were used for studies of the relation to blood pressure, since the larger size of their arteries makes cannulation easier. A branched cannula was tied into one of the common carotid arteries, with one arm leading to a pressure meter (the Tycos sphygmomanometer gauge), and the other to a flask containing anticoagulant solution (20 per cent sodium carbonate). Figure 6 shows some of the results. Cochlear responses to a tone of 1000~ are plotted as before against the left-hand ordinate scale, and blood pressure in mm. of mercury against the right-hand scale. The trachea was clamped at *a*, and both breathing and heart beat ceased at *b*.

Immediately after clamping the trachea the blood pressure rose abruptly, reached a maximum at 126 mm., and quickly fell to 25

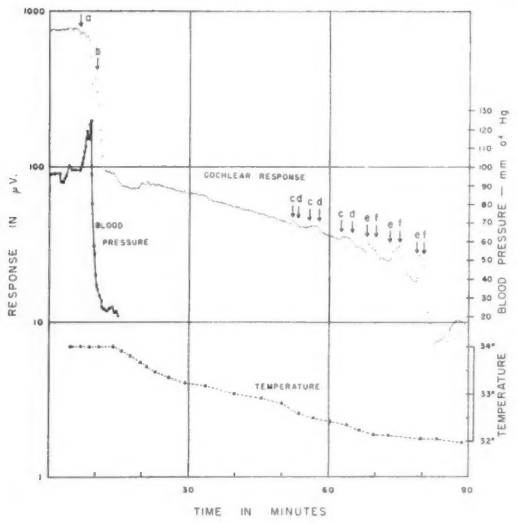

Fig. 6. Relation of cochlear responses to blood pressure and body temperature. Trachea clamped at *a*, and both respiration and heart beat stopped at *b*. Test tone, 1000~. Cat No. 251.

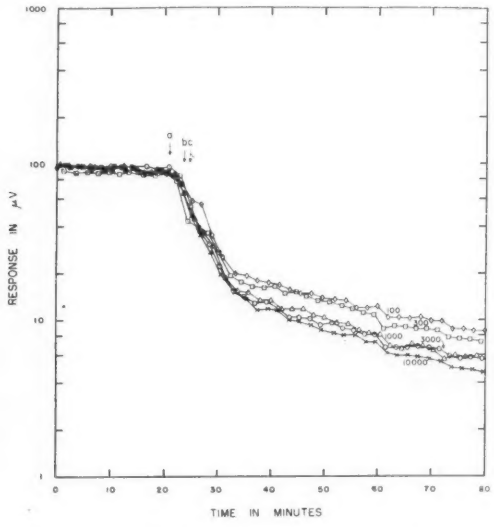

Fig. 7. Relation to stimulus frequency. Curare injected at *a*, respiration ceased at *b*, and heart stopped at *c*. Cat No. 409 R.

mm. During this time the cochlear responses were rapidly falling, except for a minor interruption in mid-course. The heart stopped when the blood pressure was recorded as 35 mm., and observations of blood pressure ended at 19 mm. as coagulation at the cannula set in.

There is no evident correlation between the cochlear and blood pressure functions.

Relation to temperature.—Figure 6 shows body temperature, as observed by rectal thermometer, during the course of the measurements of cochlear response. No correlation exists for the initial drop in the cochlear response, for it was completed before any alteration of body temperature was observed. For the later loss, however, a relationship may exist. The fall in body temperature, which began about five minutes after cardiac failure, continued uniformly during the next hour of observation, and amounted to 2 C., during which time the cochlear responses declined 20 per cent.

It is improbable that the fall in the cochlear response is due entirely to the temperature change. For one thing, the change is great: a drop of 20 per cent for a 2 loss of temperature gives a temperature coefficient of 6. For another, we know from further observations that anoxemia alone causes a reduction in response. Hence we regard the temperature effect as but one of the changes concerned in death.

That the temperature change is a significant feature is indicated by other observations made during the course of this experiment. Slight increases of response were noted at times when certain manipulations of the animal necessitated turning on a lamp over the operating table. This lamp was located about three feet above the animal, and threw a fairly concentrated beam from a 15-watt bulb. In Fig. 6 are shown some tests of this effect. The arrow at *c* indicates the time that the lamp was turned on, and *d* the time it was turned off. The effect, though slight, was consistent through three trials. At *e* a cautery also was brought near the bulla of the ear, and at *f* it and the lamp were removed. The increased heating gave larger changes. In the last trial the cautery was inserted in the opening of the bulla and brought near the bony wall of the cochlea, though without touching it; the result was a rapid and considerable rise in response and then a serious fall. As the fall began to be noticeable the application was stopped, but evidently the heat was excessive and caused damage, as only partial recovery ensued.

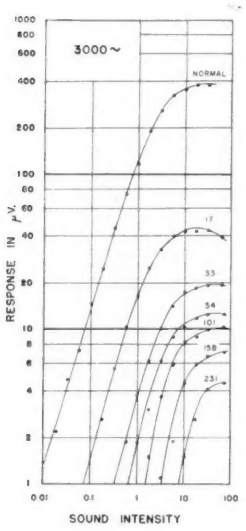

Fig. 8. Intensity functions before and after death. Test tone, 3000~. The abscissa shows sound intensity in dynes per sq. cm. Guinea pig No. 172.

It is possible that the temperature effect for the cochlear response is related to that recently shown by Weitz[3] for threshold sensitivity to pressure and vibration on the skin, but further investigation will be necessary to show the nature of the relationship.

Relation to stimulus frequency.—In some of the experiments, simultaneous functions were obtained for a number of test tones by presenting them in rotation. Figure 7 shows results for a cat in which measurements were made with five tones, 100~, 300~, 1000~, 3000~ and 10,000~, before and after killing with a dose of curare. The stimulus intensities were first adjusted to give a normal response of about 100 μv., and thereafter each was maintained at the value so determined. The rate of presentation was such that a measurement was obtained for each tone every two minutes.

Curare was administered at *a*. At *b* respiration ceased, and at *c* the heart stopped. The responses fell rapidly for about 10 minutes and then more slowly during the next 50 minutes of observation.

During the period of rapid loss, the responses for the different frequencies remained similar in magnitude, apart from a few irregularities. Toward the end of this period, however, a differential effect

began to be shown. The high frequencies suffered a somewhat greater loss than the low frequencies.

Similar results have been obtained on other animals. In general, after the period of rapid loss, the curves for different frequencies separate and run fairly distinct courses. Several instances have been noted in which the response was rising for one frequency while it was falling for another. Evidently the changes in the cochlea brought about by death do not have equal effects on the responses to different frequencies. Usually, as in the case illustrated, the high tones are most seriously affected, but this order is not an invariable one.

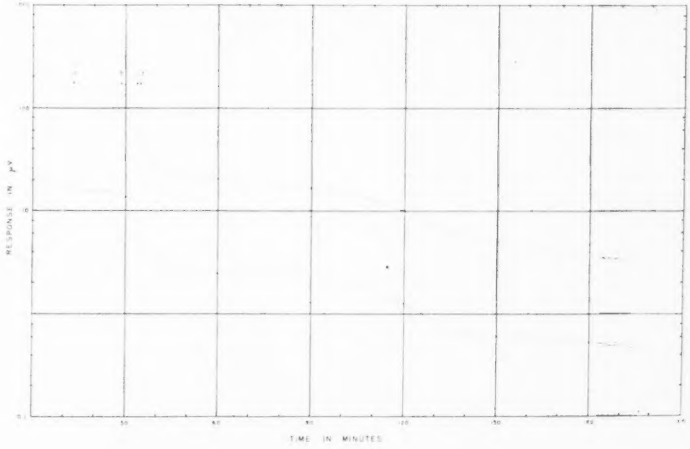

Fig. 9. Effect of stimulus intensity upon the death function. At *a* and *b* curare injected, at *c* respiration ceased, and at *d* the heart stopped. Test tone of 1000~ delivered at different intensities to the two ears; upper curve shows right ear and lower curve left ear. Guinea pig No. 265.

Relations to intensity.—The normal relation between the cochlear response and stimulus intensity is simple except at the upper end of the intensity range where overloading enters. The function is shown by the normal curve of Fig. 8. Here the stimulus had a frequency of 3000~, and was varied in intensity as shown by the abscissa. The curves to the right of the one marked "normal" represent measurements made at different times after death was produced by pithing the medulla. The time after death is indicated in minutes by the number above the curve.

It will be noted that death reduces sensitivity without causing any notable change in the form of the intensity function. The curves remain straight at low and intermediate intensities, and bend at high intensities as before. There is a suggestion in the last two curves, for 158 and 231 minutes after death, that bending is somewhat delayed, but the observations were too few to establish this point.

The question was raised whether stimulation might have an effect upon the rate of deterioration of the responses. If the action of the cells responsible for the potentials depends upon some reserve of material, or is related to a sensitizing substance, strong stimulation should accelerate the deterioration. Figure 9 illustrates an experiment made to investigate this question.

Electrodes were applied to both right and left ears, and a switch was provided for connecting each alternately with the amplifier and recording system. The right ear was stimulated with a 1000~ tone of fairly high intensity, while the left ear was stimulated with a tone of the same frequency but 20 db. lower in intensity. Both tones were applied continuously throughout the period of observation, which lasted for nearly two hours after death. The animal was killed with curare, which was administered at times shown at *a* and *b;* at *c* respiration ceased, and at *d* the heart stopped.

The curves for the two ears are almost exactly concurrent. They contain the same features of initial loss, leveling out at 60 to 100 minutes, and secondary drop beyond 120 minutes. Even a slight interruption in the initial drop at 34 minutes is evident in each.

The similarity of the curves is not perfect; careful examination will show a slight convergence, which amounts to 1.4 db. over the whole period of observation. This difference is small in relation to the difference in stimulus intensity, and hence it appears that exhaustive action as a result of stimulation is unimportant. We conclude, therefore, that the cochlear potentials arise through a direct translation of stimulus energy and not through a liberation of stored energy. Moreover, it appears that in the course of death the cellular processes are reduced in a simple linear manner, without alteration of their fundamental character.

SUMMARY

The course of the electrical responses of the cochlea was studied in guinea pigs and cats after death had been caused by each of four procedures. These were (1) pithing the medulla, (2) clamping the heart, (3) clamping the trachea, and (4) poisoning with curare.

All of these procedures produce a prompt impairment of response. Clamping the heart causes the most rapid loss, while curare poisoning produces the most moderate initial effect.

After a large initial loss, the responses decline relatively slowly, and occasionally show periods of stability and of partial recovery. Responses are still present after five hours, but not after 24 hours.

A "rebound" immediately after the initial drop is a common feature. It occurs in the absence of the middle ear and hence is not caused by relaxation of the tympanic muscles. The same is true of the later periods of partial recovery.

No simple relation has been observed between the changes of cochlear response and changes of blood pressure.

The initial fall in cochlear potentials seems unrelated to body temperature, but a relation probably exists for the later course of the change. Even slight applications of heat cause a noticeable increase in the responses.

The death function varies somewhat with stimulus frequency. After the initial drop, which is suffered by all frequencies, the curves for different tones follow slightly separate courses. Usually the high tones show the most rapid decline, but exceptions occur.

Death reduces the magnitude of responses without producing any significant variation in the form of the intensity function. Moreover, the course of the change is practically independent of the degree of stimulation of the ear. These facts indicate that in death the cellular changes are simple, and that there is no alteration of the effective pattern of stimulation. It is suggested that the cochlear potentials arise through a direct translation of stimulus energy and not through a liberation of stored energy.

PRINCETON UNIVERSITY.

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XXII

POLYOSTOTIC FIBROUS DYSTROPHY OF MASTOID COMPLICATED BY ACUTE MASTOIDITIS

JAMES MILTON ROBB, M.D.

DETROIT

Polyostotic fibrous dystrophy is an unusual type of bone dyscrasia recently described by Lichtenstein.[1] "It is a skeletal developmental anomaly affecting several or many bones with predominantly unilateral involvement. The involved bones show filling of their medullary cavities by gritty, grayish-white fibrous tissue containing trabeculae of newly formed primitive bone. The condition apparently results from perverted activity of the specific bone-forming mesenchyme. It manifests itself in childhood or early adult life and evolves slowly, pursuing a protracted course characterized by pain, deformity and a tendency to pathologic fracture of the affected bones. The osseous lesions tend to be exclusively or predominantly unilateral. Bones affected are first the long bones, and next in frequency are the bones of the skull, pelvic bones, ribs and phalanges. Roentgenographic observations show broadening or expansion of the bone, thinning of the cortex, characteristic rarefied and apparently trabeculated appearance usually erroneously interpreted as 'cystic disease', and secondary deformities of the affected bones. Blood chemistry findings are as follows: Blood calcium is normal or slightly elevated, serum phosphorous shows no deviation from normal, phosphatase value is normal to slightly elevated."

The microscopic findings described by Lichtenstein[1] are as follows: "There are small trabeculae of primitive poorly calcified new bone irregularly dispersed within the fibrous tissue without following any definite pattern. There are small trabeculae of primitive, poorly calcified new bone of variable size and contour. They are apparently developed by osseous metaplasia, without the mediacy of osteoblasts. In the relatively avascular fibrous areas the trabeculae tend to be sparse in distribution; in the more vascular areas there is usually more extensive deposition of osteoid material and fiber bone. There is little evidence of osteoclastic resorption. Deposition of calcium with the primitive new bone is variable in extent and distribution. Generally speaking, the bone is calcified poorly and in an imperfect,

spotty fashion. The basic fibrous tissue, on the whole, is relatively avascular showing only occasional thin-walled vascular spaces. The process is due to a disturbed function or development of the spongiosa and filling of the medullary cavity of affected bones by fibrous tissue in which trabeculae of poorly calcified primitive new bone are developed by osseous metaplasia. The cause of this is questionable. There was no instance of hereditary transmission of the disease."

The number of cases reported is not accurate. Lichtenstein[1] states: "A number of other cases have been reported under a bewildering variety of titles such as osteodystrophia fibrosa unilateralis, unilateral polyostotic osteitis fibrosa, unilateral Recklinghausen's disease, osteodystrophia fibrosa cystica generalisata limited to one side of the body, focal osteitis fibrosa, osteitis fibrosa in multiple foci, osteitis fibrosa with formation of hyaline cartilage and osteitis fibrosa disseminata."

He reports four cases seen by him and material sent to him from four other cases.

Horowitz and Cantarow[2] reported a case in 1939. They found a consistent absence of abnormality of calcium and phosphorous metabolism during a period of progression of the skeletal lesions. There was no abnormality of the parathyroid glands on surgical exploration of the neck. They suggest that the causes of the changes in the bones result from perverted development of the bone forming mensenchyme, and a congenital basis has been suggested. The possibility exists that there is an autochthonous peculiarity of the mesenchymal bone, but this still leaves us in the dark.

More recently, Moehlig and Schreiber[3] have reported a case of polyostotic fibrous dysplasia which involved the right parieto-occipital area, the right ilium, femur, tibia and fibula. The patient was a male, aged 16. Blood chemistry findings showed a normal calcium and phosphorous value with a slight elevation of the phosphatase level. The interesting feature of this case was definite evidence of hypo-pituitarism. The patient showed certain feminine characteristics: feminine type of breasts, feminine distribution of pubic hair, no beard, no axillary hair and a puerile voice. As to the etiology, Moehlig feels that the cause is due to a hereditary dyspituitarism which produces a unilateral mesenchymal bone defect in the form of polyostotic fibrous dysplasia. The opinion is advanced that the unilateral involvement of the skeleton is due to an unbalanced chromosomal aberration, the defect being inherited from the maternal side.

Fig. 1. Roentgenogram of the skull. Tumor involving the right parieto-occipital area, lateral surface of the skull and right mastoid area.

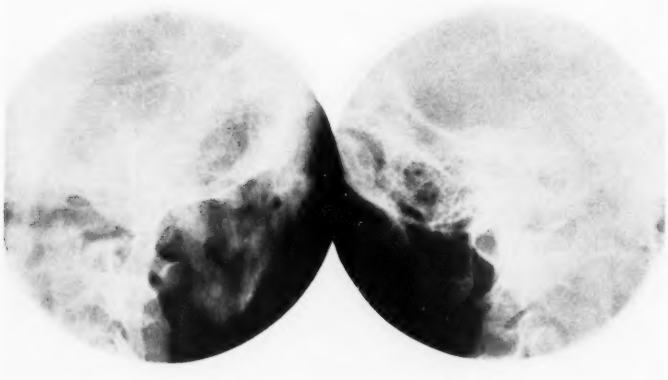

Fig. 2. Roentgenogram of mastoids showing increased density on the right side.

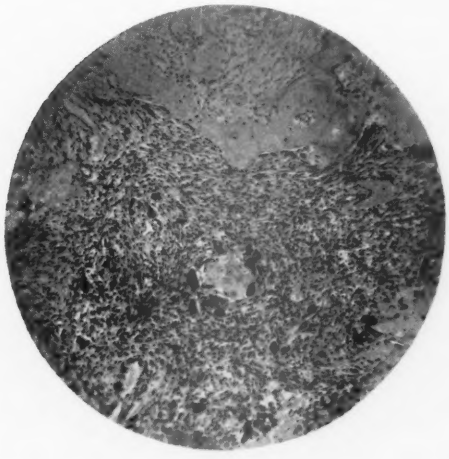

Fig. 3. Fibrous marrow with osteoid trabeculae, leucocytic infiltration, giant cells.

To these rare cases found in the literature, I have been able to add the following case:

REPORT OF A CASE

N. M., a white male, aged 20, 76 inches tall and weighing 190 pounds, was admitted to Harper Hospital on January 25, 1941. At that time he reported having had pain in the right ear for the previous six weeks, chills and fever for one week, and a mass behind the right ear for the previous four days. There was no discharge from the ear at any time.

He stated that there had been a large mass in the right parieto-occipital area and the right mastoid area since childhood. There was a gradual increase in size of these masses through the years. Five years ago he began to complain of deafness in the right ear. Examination by the family physician at that time revealed considerable obstruction of the external auditory canal, and the drum head could not be seen. Deafness progressed, and observation one year later showed complete obstruction of the external auditory canal by a bony tumor.

There was no familial history of tumors involving bone. The stature, however, is interesting and points to a definite hyperpituitarism. The father is 42 years of age and is 71 inches tall; the mother is 41 years of age and is 67 inches tall. One sister, aged 16, is 63 inches and one brother, aged 10, is 68 inches. Tallness of stature was a characteristic of the father's siblings.

A large tumor mass was found in the right parieto-occipital area measuring about 10 cm. in diameter and 4 cm. in thickness. There was a tumor mass of equal size in the right mastoid area upon which was superimposed a large sub-

periosteal abscess due to the breaking through this changed cortex of pus from a suppurative mastoid cavity. The external auditory canal was entirely obstructed. Hearing tests could not be made at this time because of the illness of the patient.

Roentgen studies of the skull, mastoids, arms, and pelvis were made by Dr. E. R. Witwer of Harper Hospital. The study of the skull revealed evidence of a large bony tumor mass arising from the right occipital ridge posteriorly. This apparently involved both the inner and outer tables. The base of this structure had a somewhat cystic appearance, and it extended down the lateral surface of the skull into the temporal and zygomatic areas, involving the mastoid structure. (Fig. 1.)

On the left side the mastoid structure was of the adult type with a very thick mastoid wall. On the right side the structure was less clearly defined, as the detail was obscured by the fibrocystic changes in the skull. There was, however, definite evidence of invasion and destruction of the mastoid process on the right side. (Fig. 2.)

Fibrocystic changes were present in the left radius. Study of the pelvis revealed slight changes in the right ilium near its sacral articulation, which simulates the bone changes seen in the shaft of the left radius. The changes described in the skull on the right side, together with findings in the left radius and right ilium are, in my opinion, associated with polyostotic fibrous dysplasia.

OPERATION

The patient was taken to the operating room the day of admission. The post-auricular incision opened a large subperiosteal abscess. The cortex was soft and spongy, and when opened, there exuded a quantity of pulsating discharge. Because of the tumor mass, distorted anatomy, and free bleeding, it was impossible to determine all the landmarks. Neither the position of the external semicircular canals nor that of the facial ridge could be determined, except in a general way, due to the fact that the bony tumor had invaded this neighborhood. This infected soft, bony tumor mastoid was curetted as thoroughly and as rapidly as possible creating an enormous cavity with considerable dural exposure. The operation could not be completed because of the serious condition of the patient. He received two blood transfusions. The patient did surprisingly well. He was returned to the operating room on January 30, 1941, and a modified radical mastoid operation was done. This modified radical operation was necessary because it was impossible to determine the course of the facial nerve through the bony tumor mass. An unusually extensive plastic operation was done so that drainage from the middle ear as well as from an enormous mastoid cavity would always be effected. Another complicating factor was that the condyloid process was so enlarged that it aided greatly in obstructing the external canal. It was impossible to remove this without invading the temporomandibular joint. The wound was packed and the patient returned to the ward in fair condition. He received another blood transfusion. Postoperative course was without complications and uneventful. He was discharged on February 8, 1941.

The consultant, Dr. Robert Moehlig, felt that this patient presented definite clinical evidence of a polyostotic fibrous dysplasia.

Blood chemistry findings on January 31, 1941, showed: Calcium 9.8 mg. per 100 cc. serum; phosphorous 3.05 mg. per 100 cc. serum; phosphatase value 2.8

Bodansky units. These were repeated on March 3, 1941: Calcium 12.9 mg. per 100 cc. serum; phosphorous 4.1 per 100 cc. of serum; phosphatase 6.2 Bodansky units.

Specimens of the tumor mass were sent to the laboratory and reports were made by Dr. P. F. Morse, pathologist of Harper Hospital. The specimen consisted of bone fragments more or less diffusely infiltrated with pus and granulation tissue. The matrix of bone was distinctly abnormal, consisting of osteoid trabeculae with increased bone resorption and areas of osteoblastic hyperplasia. There were large lacunae in which were found multiple osteoclasts. In addition to this the fibrous marrow was rapidly increasing and in the neighborhood of the purulent areas contained hundreds of giant cells so that in some limited areas a resemblance to giant cell tumor was emphasized. The picture was that of an infection in bone which had defective ability to heal and was laying down abnormal callus as a result of some metabolic disorder in the presence of an infectious process. (Fig. 3.)

Postoperatively, hearing tests were made. Hearing in the left ear was normal. With noise apparatus in the left ear, the patient heard a loud spoken voice in the right ear *ad concham*.

COMMENT

This patient showed characteristics of polyostotic fibrous dysplasia. In addition to the involvement of the right parieto-occipital area, the left radius, and the right ilium, the mastoid on the right side was involved. He developed an acute mastoiditis on the involved side, was operated on and recovered. . There seems to be definite evidence in the patient and in the family history of hyperpituitarism. This points more closely to a pituitary dystrophy as to the etiology of this disease and also to the influence of the pituitary on cranial dysplasia. This case is unusual and interesting because the disease involved the mastoid and was complicated by an acute mastoiditis.

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XXIII

SULFONAMIDE THERAPY FOR ACUTE OTITIS MEDIA AND MASTOIDITIS*

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With the introduction of new therapeutic agents such as the sulfonamide compounds, the technic for successful application of them must be slowly worked out by clinical trial. One of these compounds itself may produce certain ill effects which place an additional burden on the physician. Naive dependence on the compound may lull the usual watchfulness of the physician for the development of complications and thus work to the disadvantage of the patient.

SELF-LIMITING AND INVASIVE TYPES OF OTITIS MEDIA

Hadjopoulos and Bell[1] stated that two types of infection can occur in the middle ear. One of these is caused by obligative aerobes and may enter the middle ear through the lumen of the tube and produce an infection limited by the amount of oxygen present in the spaces of the middle ear when inflammatory swelling closes the eustachian tube.

The authors believed, however, that in the majority of cases the infection arises by invasion of a facultative anaerobe which reaches the middle ear along the submucosal lymphatic vessels of the eustachian tube. This type of organism, being able to multiply in the presence of a very low oxygen tension, produces a more dangerous infection of the middle ear and the mastoid than might otherwise occur.

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VIRULENCE OF STREPTOCOCCI

The varying severity of otitis media and mastoiditis is undoubtedly affected by variation in the virulence of streptococci and pneumococci from year to year or in various localities. In support of this view Kopetzky and Hadjopoulos[2] found that in acute mastoiditis caused by hemolytic streptococci variations occurred from year to year in the severity of the infection and also in the mortality rate. For a period of years these variations were characterized by regular periodicity, and the authors suggested that a major cycle would consist of a period of five to six years.

DEVELOPMENT OF BIOLOGIC RESISTANCE

Nitti and Bovet[3] demonstrated that mice recovering from streptococcic infections after sulfanilamide therapy were completely susceptible to new infections with the same organisms, a study which thus indicated that an immunity to infection does not develop when the infection in question is terminated by chemotherapy.

ANATOMIC ASPECTS OF THE MIDDLE EAR AND THE MASTOID PROCESS

Because of certain developmental characteristics peculiar to them, the cavities, middle ear and mastoid antrum, lying along the line of fusion of the petrous and the squamous portions of the temporal bone, are lined by a rather flat-celled layer of epithelium with an underlying vascularized mesodermal layer called "mucoperiosteum." From the walls of these cavities in all directions the systems of pneumatic cells of the mastoid process and the petrous pyramid develop. It is thus obvious, from the pathologic standpoint, that involvement of the middle ear and the mastoid antrum without some extent of involvement of the contiguous cells of the mastoid and the petrosa is improbable. There is a great variation in the degree of development of the pneumatization of the mastoid process and the petrosa; the resulting mastoid process and petrous pyramid vary from the large pneumatic-cell type through the small-cell and diploic type of structure to the sclerotic type. The type of pneumatization present may have a considerable influence on the course of an infection in the middle ear and mastoid.

TOXIC EFFECTS OF SULFANILAMIDE AND SULFAPYRIDINE

The various toxic effects which may be produced by these sulfonamide compounds have been so frequently described that it does

not seem necessary to the purpose of this paper to discuss them further.

PATHOLOGIC ASPECTS OF OTITIS MEDIA

According to Fowler,[4] invasion of the middle ear by pathogens produces edema of the mucous membrane, which swells five to ten times its normal thickness; then serous effusion into the cavity follows. Next, leucocytic infiltration of the submucosa occurs; it begins perivascularly and then extends to involve the entire mucoperiosteum. In time, material which is effused into the cavity tends to become purulent. As fluid collects in the cavity, increased hydrostatic pressure is generated, and more and more of the surrounding cells become involved. The more virulent the infection in the submucosa, the more quickly the effusions become purulent and the more reaction is produced not only in the middle ear but also in the communicating pneumatic cells. If the infection in the main cavity persists, it almost invariably produces thrombophlebitis of small veins in the mastoid process and the petrosa. Excessive quantities of fluid secreted by the mucous membrane may produce destruction of bone by direct pressure. Destruction of the epithelium at various regions also occurs, and invasion of the cavities with granulation tissue consequently is produced.

This process may regress or heal, so that a more fibrotic mucous membrane and organized bands of scar tissue attached to the ossicles remain. Usually, there is some reduction in the size of the air cavities which already exist, and among young children infection may inhibit further pneumatization of the mastoid process. Regrowth of osteoid tissue of some extent nearly always ensues after the breaking down of bone. In the pressure of progressive empyema the regrowth of bone lags behind the breaking down process, but during the healing process the converse is true. With the regrowth of bone the connections between the mastoid cells and between the cells and the mastoid antrum may be closed off. This process reduces the vascularity of already poorly vascularized deficiently anastomotic cell partitions. This is why more serious infections are likely to occur among persons who give a history of previous otitis media.

PATHOLOGICAL ASPECTS OF ACUTE MASTOIDITIS

Lillie[5] classified acute mastoiditis according to two clinicopathologic types: the osteothrombophlebitic type and the suppurative coalescent type. In the osteothrombophlebitic type the spread of infection is brought about by infective thrombophlebitis of the small

vessels of the mastoid process. It is not a stage of the coalescent type. Because of lack of sufficient blood supply, osteoclasts do not invade the bony septums and lime salts are not carried away from the bony lamellae, but the fundamental architecture of the bone is nevertheless destroyed, the bony walls becoming soft and necrotic. Symptoms of sepsis are likely to appear early in the course of the disease because of involvement of the vasa vasorum of the sigmoid sinus in the thrombophlebitic process. A serous or seropurulent discharge from the middle ear may be present, but is not necessarily a conspicuous feature in the course of the disease. Lillie pointed out, as did Beck,[6] who first described this entity, that this disease potentially is a very dangerous type of mastoiditis because, due to the spread of the infection through vascular channels, vascular and intracranial complications occur frequently without producing the usual signs of what is called "surgical mastoiditis."

In the presence of suppurative coalescent mastoiditis the infection advances primarily along the lining membrane of the air cells, and increased pressure may produce destruction of the mucous membrane and the bony trabeculae of the mastoid process. Thrombophlebitis occurs only secondarily, and even then there is sufficient remaining vascularity to permit carrying away of the lime salts by osteoclasis. This produces a cavity which is filled with pus and lined by granulation tissue. The abscess gradually enlarges as the disease process extends. The clinical course of this type of mastoiditis often is less violent than the course of the osteothrombophlebitic type of mastoiditis. This type of mastoiditis occurs more frequently in extensively pneumatized bones, and intracranial and vascular complications of the disease occur less frequently than in the osteothrombophlebitic type of mastoiditis.

It would seem unnecessary to consider herein the pathologic aspects of chronic suppurative otitis media, because it is well known that the problem in the presence of that condition is one of affording escape for a mass of cholesteatoma rather than one of combating infection.

MODE OF ACTION OF SULFONAMIDE COMPOUNDS

The exact mode of action of sulfonamide compounds is unknown. It may well be, however, that the destruction of protein with "peptone" formation and resulting inhibition of bacteriostasis as described by Lockwood[7] play important roles in the chemotherapeutic treatment of infection in such structures as the ear and the mastoid

process. Of importance also may be the fact that satisfactory concentrations of drugs cannot be obtained in tissue such as bone, where the blood supply may be inadequate. The work of Locke, Main and Mellon[8] and Shaffer[9] suggests that oxidation and reduction reactions play important parts in the action of sulfonamide compounds. Therefore, as Shaffer stated, it would be logical to assume that bacteria in the blood stream and in regions which are well supplied with blood are more exposed to the bactericidal effects of sulfonamide drugs than would be, for instance, bacteria in bony structures. Correspondingly, bacteria sequestered in tissues or situations (abscesses) which have a poor blood supply may be expected to be less accessible to the bactericidal effects of sulfonamide compounds. In general, these hypothetic observations appear to be in accord with clinical and experimental experience.

REPORTS ON THE TREATMENT OF ACUTE OTITIS MEDIA AND MASTOIDITIS

There are many favorable reports in the literature on the effects of sulfonamide compounds on acute otitis media, mastoiditis and their complications. For instance, Long and Bliss[10] stated that "an increasing amount of evidence is accumulating that acute simple hemolytic streptococcal and pneumococcal mastoiditis can be controlled by chemotherapy alone."

Horan and French[11] found that in the British navy, in some 23% of cases of acute otitis media, the condition eventuated in mastoiditis before sulfanilamide was used. In the period during which chemotherapy was being tried out this percentage decreased to 4.5.

Baker and Bradford[12] wrote that the drug was valuable in all cases of acute otitis media in which the disease was caused by hemolytic streptococci and that it probably was of value when the condition was caused by other organisms. They reported four cases of "surgical mastoiditis" in which the patients were treated with sulfanilamide. The patients recovered without surgical intervention. The authors added, however, that before the advent of sulfonamide drugs many patients suffering from acute otitis media were admitted to the hospital and yet recovered without undergoing mastoidectomy.

Goodyear[13] stated that in some cases of acute otitis media caused by hemolytic streptococci (that is, when the condition is in an early stage), sulfanilamide, when effective, produces a favorable response within from one to four days, and that when no improvement occurs within four days, administration of the drug should be discontinued

because of the masking effect the drug produces on developing complications. Some reports on the unfavorable effects of sulfonamide drugs on otitis media and mastoiditis are extant. For instance, Kopetzky[14] observed that since sulfanilamide has been available, many more patients come to hospitals suffering from epidural abscesses than was previously the case. He believed that many of these extension processes occur because sulfanilamide was used in the early stages of the otitis infection and masked the course of the disease.

Morrison[15] observed that sulfanilamide will mask the clinical signs of coalescent mastoiditis in which the inflammatory process is still active. He treated his patients who had mastoiditis with sulfanilamide, and they had no pain or mastoid tenderness when they were examined one hour previous to undergoing mastoidectomy. Yet, when the mastoid processes of these patients were opened they contained pus under pressure, from which hemolytic streptococci were cultured. Flake and Carey,[16] Cone[17] and Fenton[18] have made similar observations.

Maybaum, Snyder and Coleman[19] observed that sulfanilamide was ineffective in the presence of a suppurative focus in the mastoid process. They wrote that sulfanilamide masks the clinical evidence of mastoiditis caused by hemolytic streptococci without arresting the progress of the disease.

Kopetzky[20] stated that although the administration of sulfanilamide will clear body fluids infected by hemolytic streptococci, it does not seem to kill hemolytic streptococci lodged in an active osseous lesion. Eagleton[21] observed that sulfanilamide is not effective against organisms in encapsulated abscesses or in necrotic tissue, even when a high concentration of sulfanilamide is present in the blood and the cerebrospinal fluid. Houser[22] stated that after central necrosis has occurred it is impossible to influence the abscess already formed, and he thought the reason is that the blood containing the drug no longer reaches the region in question.

Smith and Coon[23] observed a patient suffering from suppurative coalescent mastoiditis in whom purulent meningitis developed postoperatively, caused by hemolytic streptococci. Sulfanilamide so effectively masked the clinical evidence of meningitis (except for elevation of temperature) that meningitis was discovered only accidently during performance of a Tobey-Ayer test.

Lillie[24] stated that among patients who are receiving sulfanilamide, the clinician must learn to recognize an entirely new set of

indications for surgical interference, because of the masking effects sulfanilamide exerts on the usual symptoms.

EFFECTS OF SULFONAMIDE DRUGS IN PREVENTION OF THE DEVELOPMENT OF OTITIS MEDIA

Sako, Dwan and Platou[25] treated 100 patients who had scarlet fever with sulfanilamide, and complications developed in eight of them. Five of these eight patients had acute otitis media. Among 100 similar patients not treated with sulfanilamide, complications developed in 41. Seventeen of these 41 patients had acute otitis media. Four of these 17 patients underwent mastoidectomy.

Anderson[26] studied 125 cases of measles in which sulfanilamide had been employed and concluded that there seemed to be some reduction in the incidence of otitis media in these cases as compared with the incidence of the condition in a previous series of patients who had not received sulfanilamide.

ANALYSIS OF REPORTS IN THE LITERATURE

On the bases of review of the literature and considerations of the mode of action of the drug, it would seem that the sulfonamide drugs act best in an environment in which a good blood and oxygen supply is present, one which is free of peptones and broken-down leucocytes and which is not constituted of bone.

The middle ear and mastoid process are essentially bony loci with a notably poor blood supply. A consideration of the pathologic processes suggests that inflammation would rapidly decrease the favorableness of the region to the action of sulfonamide preparations.

MATERIAL STUDIED

In attempting to analyze our results in the treatment of acute otitis and acute mastoiditis with sulfonamide compounds, we shall compare results obtained for a group of treated patients with results obtained for a comparable group of untreated patients.

Acute otitis media.—The present series consists of 265 patients who had acute otitis media. Of these, 112 received sulfonamide therapy. For the purpose of analysis we have included in this group all patients suffering from otitis media who received sulfonamide therapy, regardless of the adequacy of the dosage. The reason for this is the fact that we do not feel it justifiable to build the results of this study entirely on the consideration of adequacy of treatment.

There remain, then, 153 patients who did not receive chemotherapy. These patients therefore constitute a control series.

Of the 112 patients who received chemotherapy, 60 had an infection caused by hemolytic streptococci, and 16 patients had an infection caused by the *Diplococcus pneumoniae*. In 36 cases either no culture was obtained or no organism was identified; that is to say, infection was caused by a group of nonspecific organisms.

Among the 60 patients who had otitis media caused by hemolytic streptococci, and who received chemotherapy, the ears of 26 drained for 21 days or more. The ears of the remaining 34 patients drained for less than 21 days. Among the 16 patients whose infection was caused by the *Diplococcus pneumoniae*, the ears of three drained for 21 days or more, and the ears of 13 drained for less than 21 days. Among the 36 patients whose infection was caused by nonspecific organisms, the ears of 10 drained for 21 days or more, and the ears of 26 drained for less than 21 days.

In the entire series of 112 patients who were treated with sulfonamide drugs, therefore, it is seen that the ears of 39 (35%) drained for 21 days or longer and that the ears of 73 patients (65%) drained for less than 21 days.

Among the 153 patients who did not receive chemotherapy, there were 34 (22%) from whom hemoyltic streptococci were isolated, 15 patients (10%) from whom the *Diplococcus pneumoniae* was isolated, and 104 patients (68%) concerning whose infection either culture was negative or no culture was made; that is to say, they had infections caused by nonspecific organisms.

The ears of 19 untreated patients (56%) from whom hemolytic streptococci were isolated drained for 21 days or more. The ears of the remaining 15 untreated patients (44%) from whom hemolytic streptococci were isolated drained for less than 21 days.

The ears of six (40%) of the 15 untreated patients from whom the *Diplococcus pneumoniae* was isolated drained for 21 days or more, and the ears of the remaining nine patients (60%) drained for less than 21 days.

Among the 104 untreated patients whose infection was caused by organisms of a nonspecific group, the ears of 22 (21%) drained for 21 days or more, the ears of 82 patients (79%) drained for less than 21 days.

For the entire series of 153 patients who did not receive chemotherapy, therefore, it is seen that the ears of 47 patients (31%) drained for 21 days or more and that the ears of 106 patients (69%) drained for less than 21 days.

In any comparison of results obtained for the group receiving chemotherapy with results obtained for the group not receiving chemotherapy, it should be remembered that these statistics may be influenced by the fact that patients who had milder otitis media tend to be included in the untreated group.

Mastoiditis as a sequel to otitis media.—It will be recalled that of the 112 patients who received chemotherapy for otitis media, there were 60 whose infection was found to have been caused by hemolytic streptococci. Twenty-seven (45%) of these 60 patients had "surgical" mastoiditis as a sequel to otitis media.

It will be recalled, similarly, that among the 153 patients who did not receive chemotherapy, 34 were found to have otitis media caused by hemolytic streptococci. "Surgical" mastoiditis developed in 20 (59%) of these 34 patients. This percentile difference of 14 (59% compared to 45%) in favor of the treated patients, among those patients whose infection was caused by hemolytic streptococci, indicates that a moderate protection is offered the patient against the possible development of "surgical" mastoiditis by the administration of sulfonamide drugs.

Among the 16 patients who received sulfonamide therapy and whose otitis media was caused by the *Diplococcus pneumoniae*, "surgical" mastoiditis developed in three (19%). Among the 15 patients whose otitis media was caused by the *Diplococcus pneumoniae* and who did not receive chemotherapy, "surgical" mastoiditis developed in six (40%).

Among the 36 patients from whom no organism was isolated and who received chemotherapy, "surgical" mastoiditis developed in eight (22.2%). Among the 104 patients from whom no organism was isolated and who did not receive chemotherapy, "surgical" mastoiditis developed in 13 (12.5%).

COMMENT

It would appear, therefore, after examination of the results described herein, that in our series of patients there was no marked difference in the duration of drainage in acute otitis media but some

protection against the occurrence of "surgical" mastoiditis achieved by chemotherapy for those patients whose infection was caused by hemolytic streptococci as compared to those from whom no organism was isolated.

A well marked protection, however, against the development of "surgical" mastoiditis appeared to follow institution of chemotherapy for the patients whose infection was caused by one of the members of the *Diplococcus pneumoniae* group.

It must be pointed out, however, as emphasized previously herein, that we did not take into consideration the question of adequacy of dosage as a factor in the possible outcome of the disease among patients receiving chemotherapy as against outcome of the disease among those who did not receive chemotherapy. These results undoubtedly are affected by the fact that adequately and inadequately treated patients were classed together in the group of patients who did receive chemotherapy.

Choice of drug and dosage.—At the present time sulfanilamide is the drug of choice in infections caused by hemolytic streptococci. At the time this survey was made sulfapyridine was the drug of choice in infections produced by pneumococci and staphylococci, but it now appears that sulfathiazole may offer some advantages over sulfapyridine in the treatment of pneumococcic and staphylococcic infections.

It is obvious that no set rules for administration of drugs will apply to the treatment of all patients who have varying degrees of infection, but, in general, an initial dose of 30 grains (2 gm.) of the drug may be administered to adult persons, followed by 15 grains (1 gm.) administered every four hours. In the presence of more severe infection it might be well to administer an initial dose of 60 grains (4 gm.) of the drug instead of 30 grains (2 gm.) For small children the daily dose usually can be calculated on the basis of 1 to 1.5 grains (0.065 to 0.1 gm.) per pound of body weight, and a half of this total daily dose may be administered as an initial dose.

It is important to emphasize the fact that it is advisable in all types of infection similar to those under consideration herein to prevent exacerbations, to continue administration of the drug daily, in some such dosage as a half the therapeutic dose, for as long as ten days after the temperature has returned to normal.

Statistical advantages of sulfonamide therapy.—Forty-eight patients whose infection was caused by hemolytic streptococci received well-controlled (in other words, "adequate") therapy with sulfanil-

amide in the hospital, and check was made of the concentration of sulfanilamide in the blood of these patients. Therapy was stopped for six (12%) of these 48 patients because of the development of anemia or leucopenia. Of these six patients, one (17%) required mastoidectomy. The remaining 42 patients (88%) continued to receive sulfanilamide until the otitis media and mastoiditis cleared up, or until it was considered that mastoidectomy was required. Of these 42 patients, 19 (45%) required mastoidectomy. Of the whole group of 48 patients who received "adequate" sulfanilamide therapy, therefore, 20 (42%) required mastoidectomy. This figure (42%) may be compared with that for the 34 nontreated patients whose infection was caused by hemolytic streptococci, in 20 (59%) of whom "surgical" mastoiditis developed. The result is an advantage of 17% in favor of the 48 adequately treated patients over the 34 patients in the untreated group.

It may be pointed out that of all the patients treated, those whose infection was caused by hemolytic streptococci constituted the only adequately treated group sufficiently large to justify separate statistical study.

CONCLUSIONS

Although on the basis of theoretic considerations there would seem to be little reason to expect sulfonamide therapy to exert a favorable effect on acute otitis media or mastoiditis after the first two to four days of the disease, a slightly more favorable result was obtained for patients who received sulfonamide therapy than for the group of patients not so treated. That such improvement is more apparent than real is suggested by the fact that "surgical" mastoiditis developed with nearly equal frequency in the group of patients receiving so-called adequate dosage and in the group of patients who received sulfanilamide therapy without regard to adequacy of dosage. This observation is based on an analysis of the cases in which hemolytic streptococci were the causative organisms. However, in the group of patients in whom the disease was produced by pneumococci, the administration of sulfonamide drugs produced an unquestionable advantage. These results are probably referable to the fact that most of the patients in whom the disease was produced by both pneumococci and streptococci were receiving adequate doses, although values for sulfanilamide in the blood were not obtained concerning all these patients.

If therapy with sulfonamide drugs in the presence of acute otitis media or mastoiditis in which the disease is caused by streptococci

is contemplated, the fact should be considered that in our experience, at least, administration of the drug had to be discontinued for more than 10% of the patients who received "adequate" dosage because it produced toxic effects. Furthermore, it appears that in patients receiving sulfonamide therapy little or no biologic resistance to the infection develops; thus, on discontinuance of the therapy, if surgical intervention seems necessary, several days should be allowed to elapse so that the body may develop some localization of the infection. Surgical treatment undertaken too soon may produce a marked systemic reaction caused by dissemination of infection. These disadvantages should be weighed against the definite but slight diminution in development of "surgical" mastoiditis among those who received sulfonamide therapy in our series.

It would seem that the treatment of acute otitis media and mastoiditis with sulfanilamide should be a hospital procedure, carried out under the most careful observation of otologists and internists.

THE MAYO CLINIC.

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XXIV

THE EAR IN EXPERIMENTAL VITAMIN A DEFICIENCY*

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In contrast to the poor clinical results from vitamin therapy in otologic practice, controlled animal experiments contine to throw new light on the biologic effects of the vitamins and to suggest possible relationships between them and various otologic conditions. From this standpoint the effect of Vitamin A depletion on the ear as first described by Mellanby[1] is particularly important. In earlier experiments[2] relating to Vitamin A depletion and widespread degeneration of peripheral afferent nerves he noted degenerative changes in the central stump of the cochlear and vestibular nerves along with changes in the brain stem and spinal cord. He further observed that some of these young animals became inattentive and failed to respond to the call of people at close range. These animals also displayed incoordinate movements of locomotion.

Investigating more closely these eighth nerve changes he found striking pathology in the temporal bones of such animals. There was extensive hyperplasia of the periosteal layer of the labyrinth capsule in the internal acoustic meatus and masses of new bone in the modiolus. This resulted in narrowing and elongation of the meatus with compression and elongation of the nerves which in turn caused degenerative changes of the nerve fibers and ganglion cells. The overgrowth of periosteal bone was limited to the cranial aspect of the temporal bone and appeared to involve the base of the skull. This general involvement of the skull base and possibly of the spinal canal with its associated narrowing of foramina might be the direct cause for the widespread nerve involvement observed by Mellanby. His observations on the temporal bones of dogs have been confirmed on rats by Loch[3] and by Covell.[4] All the above observations have been concerned chiefly with histopathologic changes. No quantitative

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tests of function were carried out in these animals. It appeared indicated therefore to extend the observations by including quantitative tests of cochlear function that could be correlated with the histopathologic changes in the temporal bone.

METHOD

Litters of rabbits about eight weeks old were used. As an index of cochlear function, the acoustic reflex contraction of the tensor tympani muscle was employed. Under sterile precautions the left bulla was opened and a threshold curve of muscle contraction was obtained for octave frequencies between 128 and 4096 cycles. The animals were then placed on a diet depleted of Vitamin A. The diet was made rich in cereals since Mellanby believed that this increased the amount of pathological change in the temporal bone. The diet consisted of a mixture of four parts oats to one part bran, dessicated alfalfa, calcium carbonate and lemon juice. The precursors of Vitamin A in the alfalfa were destroyed by heating. This was confirmed by quantitative determinations of Vitamin A and its carotenoid precursors. The method was based on the antimony trichloride reaction evaluated by a photoelectric colorimeter. As tested in this way the diet was entirely free of Vitamin A or its carotenoid precursors. This quantitative test for Vitamin A was also applied to the blood plasma. Vitamin D was not added in this experiment. Mellanby added Vitamin D in the form of irradiated ergosterol. The animals were kept on this diet for four to eight months and developed disturbed function of the extremities, xerophthalmia, keratomalacia and a poor nutritional state. They were markedly underweight and failed to grow normally. The experiment was terminated by again testing the threshold of the acoustic tensor tympani reflex on both sides and drawing blood for quantitative determination of Vitamin A. Then the temporal bones were removed and prepared for sectioning.

A number of control animals were followed in a similar manner.

RESULTS

Vitamin level. Representative figures for Vitamin A level in the blood plasma (international units per 100 cc. of plasma) of depleted and control animals appear in Table I.

TABLE I

Control No. 51	276.3	Depleted No. 76	20
Control No. 52	340	Depleted No. 84	12.3
Control No. 53	216	Depleted No. 93	10

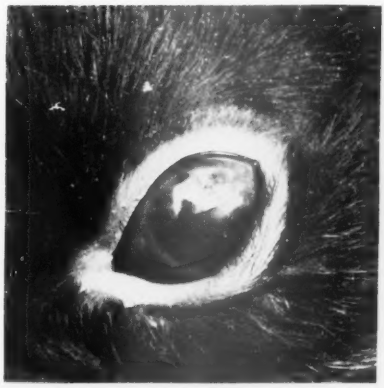

Fig. 1. Photograph of the eye of a young rabbit after about five months on a Vitamin A depleted diet. The classical eye changes of xerophthalmia and keratomalacia are most marked in the irregular white area in the cornea. These changes in the cornea are thought by Mellanby to be secondary to changes in its innervation.

The classical eye changes developed in these Vitamin A depleted rabbits (cornification of the cornea, ulceration and infection) are illustrated in Fig. 1. These changes begin to appear after about five months on the depleted diet.

Cochlear function. None of the depleted animals was deaf as tested by the acoustic tensor tympani reflex response. Only slight differences in the threshold of this response before and after depletion were noted. These differences were within the limits of experimental error in reading the threshold of contraction of the tensor tympani muscle. An average of the threshold readings from both ears was used. The maximum difference in the threshold readings for the two ears was 20 decibels. All of the depleted and control animals showed a brisk reflex response for both tensor tympani at the end of the experiment. Natural death of the animal or middle ear infection prevented muscle readings in a few instances.

Representative threshold levels for the acoustic reflex of the tensor tympani muscle before and after Vitamin A depletion and in control animals appear in Table II.

TABLE II

THRESHOLD OF ACOUSTIC TENSOR TYMPANI REFLEX FOR AIR CONDUCTED SOUND AT BEGINNING OF EXPERIMENT (a) LEFT EAR AND AT CONCLUSION (b) AVERAGE OF BOTH EARS.

		128	256	512	1024	2048	4096	8192
Control	a	60	65	70	60	40	47	
No. 51	b	55	60	67	65	35	37	
Depleted	a	60	55	72	65	35	35	
No. 76	b	60	67	75	72	45	42	
Depleted	a	60	65	70	60	45	50	
No. 93	b	53	58	65	60	33	38	
Depleted	a	60	70	75	60	37	40	
No. 83	b	55	60	65	65	45		

Vestibular function. This was not tested. The depleted animals showed unsteadiness in gait, some extensor tonus and occasionally torsion of the neck. How this was brought about was not determined but other observers relate it to pathology in the peripheral nerves or in the vestibular system. Mellanby found that the efferent nerves are much more resistant than the afferent nerves to the degenerative changes produced by Vitamin A depletion.

Histopathology. a) *Cochlea.* The most striking pathology was the extensive new bone formation in and adjacent to the internal acoustic meatus. This new bone formation is in contrast to the general arrest in growth of the long bones. The pathologic picture may well be described as a marked hyperplasia of the periosteal layer of the otic capsule on its cranial aspect. (See Figs. 2 and 3 and compare with normal in Fig. 4). The new bone was not unlike the older periosteal otic capsule but stained more pink with the hematoxylin and eosin stain. A sharp line of demarcation could be seen between the old and new bone. This probably resulted from the fact that the otic capsule had stopped growing before the experiment was begun and the new bone was applied to this older inactive bone. The new bone had more and larger vascular spaces and more haversian systems than the older periosteal layer of the otic capsule and thus appeared less compact and more active. The layer of new bone closest to the old bone was most compact and resembled most the old capsule bone. Some of the new bone contained spaces filled with fat marrow. Figure 4 represents the normal rabbit cochlea. The amount of new bone formation was dependent on the duration of the experiment (Fig. 5—compare with Figs. 2, 3 and 4) and was symmetrical for both ears. There was no new bone in the modiolus or in the scalae

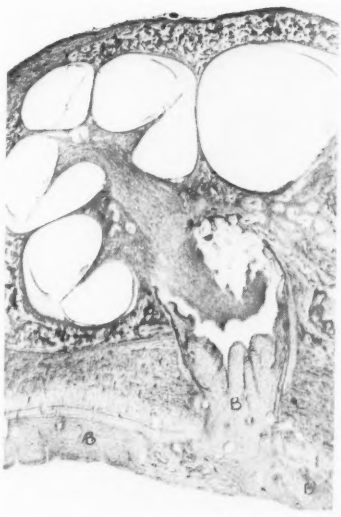

Fig. 2.

Fig. 3.

Fig. 2. A mid-modiolar section through the cochlea (X30) of a rabbit raised on a diet depleted of Vitamin A. New periosteal bone *(B)* occludes the meatus at this level (at a higher level the meatus is open) and is applied to the cranial aspect of the otic capsule. The neural elements of the cochlea are preserved, and good cochlear function was present.

Fig. 3. Section (X30) through lower portion of the internal acoustic meatus of a young rabbit raised for seven months on a diet depleted of Vitamin A showing the extensive new bone *(B)* filling the meatus at this level and extending over the posterior fossa surface of the bone. At a higher level the meatus was only partially occluded. The nerve fibers within the meatus, the cells of the spiral ganglion, and the fibers in the spiral lamina appear to be normal and cochlear function was not impaired.

of the cochlea as Mellanby described. This probably indicates a smaller degree of pathologic change rather than an essentially different type of reaction between the dog and the rabbit. In striking contrast, the bone of the otic capsule on the middle ear side showed no change. A very small amount of new bone in nodules could be seen along the walls of the cochlear aqueduct. This did not obstruct the aqueduct. The new bone appeared to extend for some distance on the cranial aspect of the temporal bone and beyond the limits of the block from which the sections were cut. There was no immature bone or thick layers of osteoid and no bone absorption by osteoclasts.

Fig. 4.

Fig. 5.

Fig. 4. A mid-modiolar section (X30) of the ear of a rabbit raised on a normal diet showing the normal width of the internal acoustic meatus and the normal arrangement of the nerve elements within the meatus. The thickness of the periosteal layer of the otic capsule in and adjacent to the meatus is in marked contrast to that of the Vitamin A depleted animals.

Fig. 5. Section through the cochlea (X30) of a young rabbit kept on a Vitamin A depleted diet for four months. Note the relatively small amount of new bone *(B)* about the sides of the internal auditory meatus and the normal arrangement of neural elements within the meatus. This section is to be compared with those in Figs. 2, 3, 6, 7, 8 from animals kept on the depleted diet for a longer time and shows that the amount of new bone formation is dependent on the length of time the animal remains on the depleted diet.

This supported the impression that the new bone was being formed slowly, that it was relatively stable, and that it was not replacing older bone.

b) *Nerve changes.* Narrowing and lengthening of the internal acoustic meatus by this new bone caused compression and stretching of the nerves in the meatus. (See Figs. 6, 7, and 8.) In spite of this, and in contrast to the findings of Mellanby, no widespread degeneration of the fibers was seen in the sections stained with hematoxylin and eosin. The fibers were present in large numbers and in normal density. Special myelin stains (Marchi) could not be used,

Fig. 6.

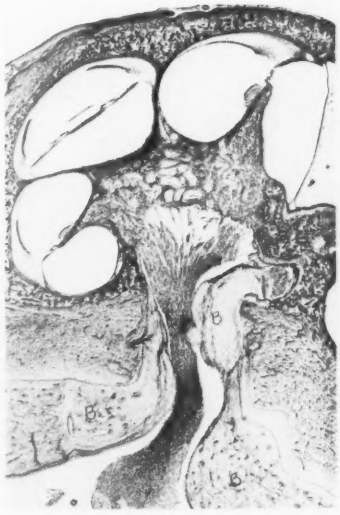

Fig. 7.

Fig. 6. Section (X30) through the cochlea of a rabbit raised on a diet depleted of Vitamin A and showing the extensive new bone formation *(B)* in the internal meatus and on the cranial aspect of the otic capsule. Note the normal capsule bone *(C)* on the middle ear aspect of the labyrinth and the preservation of the neural elements.

Fig. 7. Section through the cochlea (X30) of a young rabbit raised for eight months on a diet depleted of Vitamin A. Note the large amount of new periosteal bone *(B)* on the cranial aspect of the capsule, narrowing and elongating the internal acoustic meatus and thereby compressing and stretching the nerve elements in the meatus. Compare with the normal in Fig. 4. A distinct line of demarcation between the old otic capsule bone and the new bone can be seen. The neural elements are very little effected, and good cochlear function is present.

and therefore early degenerative changes in the nerve probably escaped detection. In this regard it is noteworthy that because of the relatively great thickness of the myelin sheath considerable compression of the nerve fiber can occur without affecting the minute axis cylinder. However dissolution of some fibers and injury to others must be strongly suspected in explaining degenerative changes seen in some of the cells in the spiral ganglion. The cochlear ganglion in the modiolus was not directly compressed by new bone as was the vestibular ganglion in the internal auditory meatus. In only one

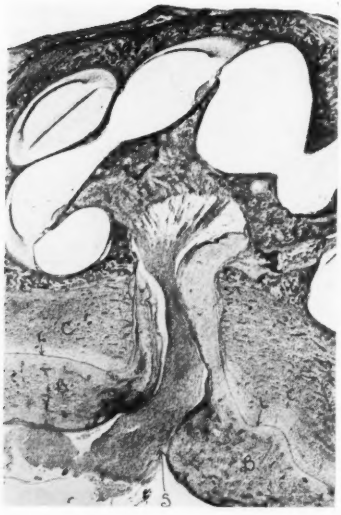

Fig. 8. Section through the cochlea (X30) of a young rabbit raised for seven months on a diet depleted of Vitamin A. The line of demarcation *(L)* between the new periosteal bone *(B)* and the old capsule bone *(C)* is very distinct. The internal acoustic meatus is narrowed and elongated with compression and stretching of the neural elements. Some of the cells of Scarpa's ganglion *(S)* appear at the mouth of the meatus. Good cochlear function was present.

preparation (Fig. 9) there was marked degeneration of the peripheral fibers supplying the lower part of the basal coil with preservation of the sheath cells. A section through the normal rabbit cochlea is illustrated for comparison in Fig. 10. The peripheral branch of a nerve is probably more susceptible to injury of the nerve cell than the central branch. This degeneration was probably secondary to degeneration of the corresponding spiral ganglion cells, but even at this level, many ganglion cells could be seen. The amount of degeneration paralleled the amount of new bone formation and the degree of compression of the nerve fibers in the internal auditory meatus. There was no widespread dissolution of ganglion cells as appeared in Mellanby's preparations.

In contrast to the observations of others, the hair cells in the organ of Corti, the cells in the stria vascularis and the fluid spaces

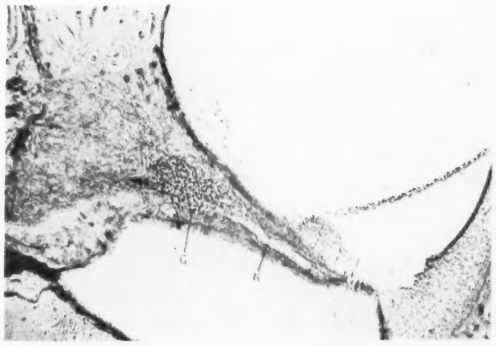

Fig. 9. Section through the lower end of the basal coil of the cochlea (X80) of a rabbit raised on a diet depleted of Vitamin A showing marked atrophy of the nerve fibers *(N)* in the spiral lamina and some changes in the spiral ganglion *(G)*. The rest of this cochlea did not show these changes, and good cochlear function was present as tested by the acoustic tensor tympani reflex.

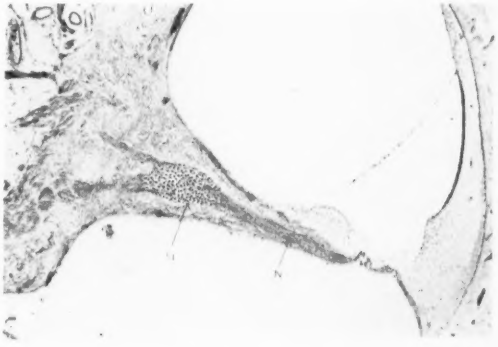

Fig. 10. Section through the lower end of the basal coil of the cochlea (X80) of a rabbit raised on a normal diet showing a normal spiral ganglion *(G)* and normal density of nerve fibers in the spiral lamina *(N)* going to the organ of Corti.

appeared to be normal. This again may be a difference in the degree of change related to the smaller amount of new bone formation in these rabbits compared with that in dogs. The amount of new bone in some of Mellanby's dogs was so great that not only was there a direct effect on the nerve elements but probably secondary effects due to interference with the blood supply of the labyrinth through compression of the internal auditory artery.

c) *Vestibular system.* Compression and stretching of the vestibular nerve and Scarpa's ganglion (see Figs. 7 and 8) by the new bone in the internal acoustic meatus resulted in changes in some of the ganglion cells. These changes were in general similar to those seen in the spiral ganglion. The density and character of the nerve fibers appeared normal in spite of compression. They had not disappeared as in Mellanby's preparations. This difference between our preparations and Mellanby's is again one of degree rather than a difference in the type of change. The peripheral fibers going to the vestibular end organs appeared to be normal in number and structure. There was no striking change in the cells of the maculae or cristae of the vestibular apparatus.

d) *Flocculus.* The new bone extended to the cavity of the flocculus, and invaded the flocculus itself. Most of the new bone was laid down as finger-like projections and as nodules at the opening into the flocculus cavity about the anterior vertical canal, and this resulted in narrowing of this opening and compression of the stalk of the flocculus. (See Fig. 11 and compare with a similar section through the normal rabbit illustrated in Fig. 12.)

e) *Middle ear.* The middle ears and bullae of these Vitamin A depleted rabbits were everywhere normal. A few animals had infected middle ears, but there was no increased incidence of otitis media over the control animals. This is in contrast to the findings in rats where a disposition to middle ear infections was observed by Loch and by Covell. Inflammatory changes in the middle ear mucous membrane and periosteum along with a thin layer of new bone on the promontory were described by them and attributed to the lack of Vitamin A. Such new bone formation is not peculiar to Vitamin A depletion but is seen as a result of periosteal irritation in otitis media from any cause. There was no hyperplasia of the bone of the bulla and middle ear cavity in the non-infected rabbits. This is in sharp contrast to the new bone on the cranial side of the otic capsule. The bulla wall opened at the beginning of the experiment for threshold reading of the muscle healed in a normal manner. Variations in experimental results in different animals (i.e., predispostion to middle

Fig. 11. Section at the level of the flocculus (X30) showing the new bone *(B)* narrowing the mouth of the flocculus cavity *(M)* and entering the substance of the flocculus. The new periosteal bone is applied to the older periosteal layer of the otic capsule throughout its cranial aspect only. Note the lack of change in the capsule bone facing the middle ear.

Fig. 12. Section at about the same level as in Fig. 11 of the flocculus *(F)* (X30) of a normal rabbit showing the width of the mouth of the flocculus cavity *(M)* and the normal distribution and thickness of the periosteal layer of the otic capsule *(P)* on its cranial aspect.

ear infections) and differences in the life span of these animals as related to the duration of the experiment emphasize the difficulties that are encountered in attempting to transpose the results of animal experiments to the clinic.

DISCUSSION

The new bone formation appears to be the basic pathologic process in the temporal bone. The degenerative changes in the nerve fibers and ganglion cells are apparently secondary to compression and stretching of the nerve. The amount of new bone formation observed in these young rabbits raised on a diet depleted of Vitamin A and rich in cereals is less than that observed by Mellanby in similar experiments on the dog. The absence of new bone in the modiolus and maintenance of an adequate blood supply to the labyrinth probably explains the lack of extensive degeneration of the eighth nerve fibers and the maintenance of good cochlear function as tested by the acoustic tensor tympani reflex. Good cochlear function was maintained in the face of degenerative changes seen in some of the spiral ganglion cells. Almost complete disappearance of ganglion cells and nerve fibers in the temporal bone sections demonstrated by Mellanby undoubtedly would lead to profound or complete loss of both the cochlear and the vestibular functions. Our findings on the other hand indicate the degree to which the cochlear nerve fibers may be compressed and the amount of change in the spiral ganglion that can occur without affecting cochlear function as tested by the acoustic reflex response of the tensor tympani muscle. This is in line with clinical findings in patients with eighth nerve tumors. Acoustic neuromas usually arise from the vestibular branch of the eighth nerve and may destroy vestibular function without greatly effecting cochlear function, although on examination either at operation or on sectioning, the tumor will be seen to compress and stretch all the nerve fibers in and adjacent to the meatus. This is particularly true of the facial nerve, which may be compressed into a microscopically thin ribbon on the capsule of the tumor without producing facial paralysis. The great thickness of myelin compared to the axis cylinder permits a great deal of compression without affecting the axis cylinder itself, and this may explain retention of function of the nerve fibers in the face of marked compression. The pathologic changes produced in the temporal bones of animals depleted of Vitamin A have not been found in human temporal bones. In the literature, a few isolated cases of bone hyperplasia in and near the internal meatus in the human are described. (See Moos and Steinbrügge,[5] Flesch.[6]) The case described by Manasse[7] is probably most sugges-

tive of similarity. His patient was 83 years old and had symmetrical hyperplasia of the periosteal bone in and adjacent to the internal meatus. The meatuses were extremely narrowed. The skull was generally thickened, particularly at its base, but there was no involvement of the otic capsule on its middle ear aspect, or of the bone of the middle and outer ear. He did not examine the temporal bone histologically, and there were no functional tests. Hypertrophy of the middle ear aspect of the otic capsule to involve the windows of the labyrinth is described by Nager[8] as part of the pathology of endemic cretinism.

The condition of severe Vitamin A deficiency in children might be considered as comparable to experimental conditions described here. Such cases with xerophthalmia have been reported along with autopsy findings,[9] but no mention of auditory or vestibular function appears in the reports, and no temporal bone studies have been made. Positive experimental results both for widespread peripheral afferent nerve degeneration and for the changes in the temporal bone appear to be regularly obtained only when young growing animals are used. This probably explains the negative results of other workers when attempting to repeat Mellanby's work with adult animals (i.e., Grinker and Kandel[10] with the monkey).

The information obtained from Vitamin A depletion experiments on these young animals cannot be immediately translated to definite clinical entities in otology but is important chiefly because it increases our knowledge of the specific factors that may influence new bone formation in the labyrinth capsule during the growing period. Knowledge of the factors influencing bone formation in the otic capsule will ultimately form a basis for a better understanding of the otosclerosis problem.

CONCLUSIONS

Young rabbits raised on a diet depleted of Vitamin A develop extensive hypertrophy of the periosteal layer of the otic capsule on the cranial aspect, including the internal acoustic meatus, posterior fossa surface and mouth of the flocculus. The overgrowth of mature lamellar periosteal bone in the internal acoustic meatus results in narrowing and elongation of the internal acoustic meatus with compression and stretching of the nerve fibers and Scarpa's ganglion in the meatus. In spite of this compression and stretching good cochlear function was retained. This was demonstrated by threshold studies on the acoustic middle ear muscle reflex.

The compression and stretching of the nerve resulted in various degrees of degenerative changes in some of the cells in the vestibular and cochlear ganglion, and in one case degeneration of the peripheral fibers to part of the basal coil.

There was no evidence of serous labyrinthitis or of degeneration of Corti's organ, the vestibular end organs or the stria vascularis.

The structures of the middle ear including the adjacent labyrinth bone were unaffected.

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XXV

THE REACTIONS IN THE EAR TO SOUND*

A. G. POHLMAN, M.D.

LOS ANGELES

In a paper on the middle ear prosthesis read before this society last year, it was indicated that the accepted interpretation of the reactions in the ear to sound was suffering from excesses of physics and from too much conjectural evidence. There was a time when opposition to the teachings of Galen was regarded as heresy. Today while the dictum of some authority may attract attention, the factual evidence submitted should be carefully examined and evaluated before the conclusions are accepted. We may be obsessed with the idea that the mechanics of hearing must be an extremely complicated reaction, and being convinced of this, we close our minds to the serious defects in the accepted explanation. The problem of how we hear is not merely one of purely academic interest. It is directly related to the proper evaluation of the results obtained through auditory tests and to possible advances in the treatment of disabilities in hearing.

The accepted interpretation of the reactions in the ear to sound holds that the conduction of vibrations into the cochlea and the capacity of the end organ to separate a complex sound into its several component frequencies are to be explained on a purely physical basis. May I quote from the comprehensive textbook on hearing by Stevens and Davis, page 276: "We shall be able completely to account for the dynamic behavior of the cochlea in response to an acoustic disturbance only when we shall have succeeded in setting up and solving the differential equations describing the motions of the various parts of the cochlear system and in evaluating the several constants involved." This statement will not necessarily be received with enthusiasm by an otologist whose interest lies in auditory disabilities rather than in higher mathematics. For my own part I would like to see the "motions of the various parts of the cochlear system" demonstrated before I go back to school to study differential

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equations and vector analysis. We are aware that excellent methods of differential diagnosis and treatment of auditory disabilities were established empirically long before the problem of the reactions in the ear to sound were considered. Indeed even today several outstanding contributions have been made, not on account of the vast amount of applied research on audition, but rather in spite of it.

The purpose of this paper is to show that the accepted explanation of the reactions in the ear to sound is for the most part incorrect. Obviously, a brief review such as this must be restricted to fundamentals, and no attempt will be made to discuss details. The problem may be presented in the form of a simple diagram which will visualize the reactions and will make it possible for the reader to judge for himself as to the validity of the objections proposed and to separate conjectural from factual evidence.

In 1851, shortly before the discovery of the end organ by Corti, the eminent biophysicist, E. H. Weber, made an interesting observation on an ear specimen. He found that when the stapes was pushed into the oval window the round window membrane bulged outward into the tympanic cavity. He assumed that the reactions in the cochlea to sound must be similar to those he had demonstrated in the specimen and proceeded to correlate this assumption with the then-known anatomy. The explanation he offered was seemingly so obvious that a sort of scientific miracle came to pass because the acoustic whale not only swallowed Weber's Jonah intact, in spite of certain physical impossibilities, but has stomached it for 90 long years. The situation, in my opinion, therefore calls for an emetic rather than for a slide rule and a table of logarithms. The fact that one can drive a truck around the block at five miles an hour is not evidence that it will negotiate the turns at fifty miles an hour. The fact that one opens a door by pushing on it does not mean that it will open when one says, "Boo"! Similarly the well known effect of seeing stars when struck on the eye does not carry the conviction that vision is brought about through the pressure of light waves on the retina. There is such a thing as *deductio ad absurdum*.

The diagram, Fig. 1, shows a schematic auditory apparatus where the drum membrane separates the bony external canal from the middle ear cavity. The drum membrane is connected to the oval window by the three ossicles where the malleus and incus are represented in the form of a bent lever. The internal ear is shown as a single semicircular canal and a cochlea which is unrolled. The cochlear chamber is incompletely divided into a *scala vestibuli* and a *scala*

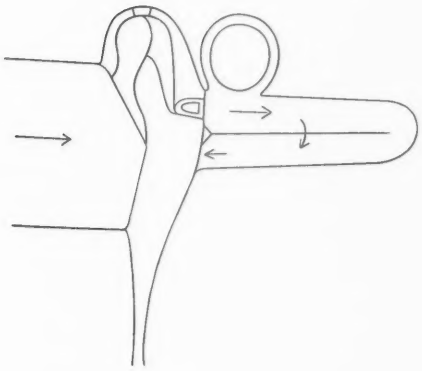

Fig. 1.

tympani by the membranous partition or basilar membrane. The *scala tympani* terminates at the round window membrane. In Weber's time it was thought that the terminal filaments of the cochlear ganglion were distributed along the length of the basilar membrane.

The Weber explanation for the reaction occurring in the middle ear is as follows: The sound entering the external auditory canal produces vibrations of the drum membrane. These vibrations are conducted through the ossicles to the oval window, and because of the lever effect of the malleus-incus the amplitudes of the drum membrane reactions are decreased in excursion and proportionately increased in power at the stapes. The efficiency in the conduction is accordingly dependent on two factors—first, the relatively large area of the drum membrane when compared to that of the stapes footplate; and second, the leverage action in the ossicles. The middle ear apparatus, therefore, has the function of a resistance-matching transformer.

When Weber applied the results of his experiments on a specimen to the reactions to sound in the cochlea, he postulated that the liquid contents could be regarded as an incompressible medium and that the dense otic capsule presented an inelastic container. Under these physical conditions some compensation area must be available to permit the liquid to shift as a whole. This compensation area was presented in the round window membrane. Accordingly, when the

stapes went in, the round window membrane bulged out and the liquid in the two scalae was displaced in opposite directions. This in turn resulted in a transverse vibrational reaction in the basilar membrane. To quote again from Stevens and Davis, page 276—"The bony labyrinth is a practically closed chamber with rigid walls, except for the oval and round windows. The fluid within it is incompressible, and therefore, when the footplate of the stapes vibrates, significant mass movements of the fluid within the labyrinth can occur only by virtue of the yielding of the round-window membrane. It is evident . . . that slow inward movement of the stapes can cause a flow of perilymph up the *scala tympani* to the round window. But there is an alternative pathway. When the movement of fluid up the *scala vestibuli* is rapid it will be opposed by the frictional resistance to flow in the narrow scala and by the inertia of the fluid-column in the apical turns. This process will generate pressure in the endolymph and hence on Reissner's membrane (which we may assume to be practically flaccid and unresisting) and on the basilar membrane beneath it. The basilar membrane will bulge into the *scala tympani,* as shown in Figure 105, and displace the perilymph within it toward the round window. The more rapid the movement, the closer to the round window is the bulge in the basilar membrane."

While Weber believed that the transverse vibrations in the basilar membrane directly activated the nerve terminals, the discovery of the end organ and the establishment of the details in its structure made it necessary to modify the explanation. It was found that the nerve terminals are distributed to the auditory cells, and further that these auditory cells are structurally similar throughout the length of the end organ. This failure of the auditory cells to show structural differences led to the assumption that they were nonspecific in their reactions and therefore behaved merely as signal stations which reported the transverse vibrations in the basilar membrane to the brain. This, however, as Helmholtz pointed out, did not account for a peripheral sound analysis. Helmholtz, therefore, assumed that the basilar membrane acted as a mechanical harmonic analyzer and that each of the fibers was tuned to react to a definite frequency. Thus, a short fiber close to the windows would react to a high frequency and activate the applied auditory cells which would signal the brain that the disturbance was located at the proximal end of the organ of Corti. A longer fiber located distally would respond to a low frequency, and the activated cells would signal this position. This explanation was the forerunner of a place theory

which was confirmed by the finding that cases of a high pitch deafness showed degeneration in the proximal end of the organ of Corti.

Unfortunately, the basilar membrane did not show dimensional differences which would make the Helmholtz theory physically possible, and something had to be done about it. So the doctrine of the selective weighting came into being. Again quoting from Stevens and Davis, page 277—"Two principal factors operate to place the disturbance of the basilar membrane closer to the round window when the frequency of stimulation is raised. 1) The basilar membrane is broadest near the helicotrema and narrowest near the round window. If the fibers of the membrane are under tension, their varying elasticity will make the longer fibers more susceptible to movement by low frequencies. The strings of a piano exhibit a crudely analogous effect. The shorter fibers will be moved most easily by high tones. 2) The mass of the total amount of fluid moved will be smaller when the disturbance is nearer to the round window. Now, in a mechanical system, the smaller the mass of the system, the higher the natural frequency. Consequently, high frequencies will tend to activate the ear in such a way as to move a small mass. Just what mass will be most readily displaced by a given frequency will depend upon the additional factors of the stiffness and resistance involved, but the general principle is clear: less cochlear fluid will be set in motion by a high than by a low frequency.

"According to these principles, aided presumably by minor factors such as variations in the physical constants of the organ of Corti, the basilar membrane will vibrate selectively at one part or another according to the frequency of the sound. This selective vibration is the fundamental physical basis of the analysis of sound by the cochlea."

This brief review of the accepted interpretation places us in a position to discuss the described reactions in the ear to sound. We will consider it step by step to determine how much is to be regarded as conjecture and how much is supported by the factual evidence. This may be done by answering certain leading questions.

First, does the drum membrane vibrate to air sound entering the external auditory canal? The answer is definitely, yes!

Second, are these drum membrane vibrations conducted into the cochlea through the ossicle chain (Weber, 1851); or do they create air vibrations in the middle ear cavity which enter the cochlea through the round window membrane (Macnaughton-Jones, 1940);

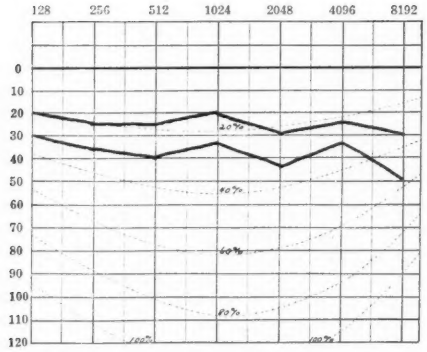

Fig. 2. Shows improvement in the sensitivity for all frequencies through occlusion of the dehiscence in the drum membrane by means of a wet cotton pellet.

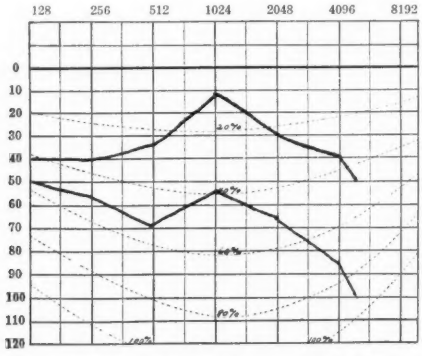

Fig. 3. Shows exceptionally great amount of increase in the air acuity due to the diaphragm-rod prosthesis.

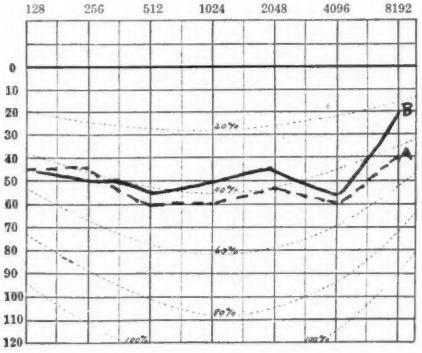

Fig. 4. The air acuity in two cases where the drum membrane and outer ossicles had been lost. Case A with stapes fixed shown in the broken line, and Case B with movable stapes in the solid line.

or is there a dual conduction where low frequencies pass through the ossicles and high frequencies through the round window membrane (Alexander, 1930)?

The answer to this question is to be found in the experimental evidence on patients with dehiscence of the drum membrane and also those in whom the middle ear apparatus has been lost or removed. The air acuity in a case with wide perforation of the drum membrane is shown in the lower line of Fig. 2. According to Macnaughton-Jones the perforation should have had no appreciable effect on the air sensitivity. According to Alexander the low tone loss would have been interpreted as a conduction deafness while the lowered sensitivity for the high tones would be due to a perception deafness. The perforation was covered by a wet pellet of cotton, and the effect is shown in the upper line. It will be noted that the sensitivity to all frequencies was increased and that there was no perception deafness as assumed in the Alexander interpretation.

Figure 3 indicates in the lower line the air sensitivity in a case where the middle ear apparatus was wanting and the more or less uniform depression characteristic of these cases. The upper line shows the improvement on introduction of a diaphragm-rod prosthesis when contact was made with the stapes. The result shows about a 10 db. improvement for low tones and at least a 40 db. increase for high tones.

The answer to the second question is that Weber was quite correct because the ossicle chain is the only effective route for the conduction of the drum membrane vibrations into the cochlea. Conduction deafness is therefore not synonymous with low frequency disabilities as formerly supposed.

Third, is the conduction of the drum membrane vibrations through the ossicles made more effective by reason of the assumed leverage action? The most recent report on the leverage action of the ossicles was submitted by Stuhlman. He found a ratio of 1.27:1 which is practically the same as that determined by Dahmann. Granting that a leverage action in the ossicles could occur to the amplitudes and the frequencies in sound vibrations, which I do not admit, then the advantage in terms of intensity would be as the inverse squares or 1.5:1. The advantage of this amount of intensity increase could not be consistently detected by a trained observer under test conditions and would therefore be of no physiological importance.

The leverage action in the ossicles, like the folding of the columella in birds, is related to a shock-absorbing function and not to an efficiency in sound conduction. The answer to question three is accordingly, negative.

Fourth, may the labyrinth liquid be regarded as an incompressible medium? The answer is definitely, no! Water contracts in volume when it is cooled, and sound is conducted through water at a considerably greater speed than through air. Then, too, to regard a liquid related to a rich blood supply as constituting an incompressible cochlear content is nothing more than physical nonsense.

Fifth, may the dense otic capsule be regarded as an inelastic or rigid container? Stevens and Davis, who agree that the container is rigid in its relation to the displacements due to air sounds, also agree it is highly elastic in reference to bone vibrations: "Experimental evidence (von Bekesy) appears to indicate that both air-conduction and bone-conduction ultimately cause similar movements of the endolymphatic fluid and of the basilar membrane in the cochlea. The air-borne vibrations arrive by way of the ossicles, whereas vibrations of the skull result in compression of the canals of the inner ear, including the labyrinth. Such compression increases the pressure in the *scala vestibuli* more than in the *scala tympani* because the round window, in communication with the *scala tympani*, is more elastic than the oval window, which is closed by the footplate of the stapes."

In other words the dense otic capsule is not a rigid container, and the Weber assumption in relation to this is incorrect. In point of fact the otic capsule is one of the most elastic of all body tissues.

Sixth, are the mass displacements in the labyrinth liquid due to an interaction between the two windows essential to audition?

The two premises upon which Weber based his interpretation of the reactions in the cochlea to sound are not facts. Let us see what happens to the further assumption that the labyrinth liquid is displaced as a mass through interaction between the two windows. May I again visualize for you the Weber explanation by means of a glass U-tube filled with water and closed at the two ends with rubber diaphragms? When pressure is exerted on one diaphragm, the other diaphragm bulges outward, and the liquid in the two arms of the U-tube is displaced in opposite directions. This is what Weber demonstrated in the specimen. If, however, one opening is fixed and pressure is applied to the yielding opening no mass displacement in

the liquid will occur, and all that could happen would be an increase in pressure and a microscopic shrinkage in the volume of the liquid. At the same time the glass tube would expand slightly. Now, if both movable windows had equal pressure applied to them, no mass displacement would take place because all shifting in the liquid would be cancelled out, and the result would be similar to what occurred in the previous experiment with only one window movable. Let us stop guessing at what might take place in terms of hearing and put the accepted doctrine of mass displacement in the cochlear liquid to the test. I have selected two cases in whom the middle ear apparatus is wanting. Both were candidates for a prosthesis. These cases were examined with an acoustic probe to determine whether or not the stapes area was sufficiently movable to accept the diaphragm-rod replacement unit. Case A was repeatedly examined with the acoustic probe and failed to reveal a movable stapes. Case B was one in which the round window faced lateralward, and both the stapes footplate and the round window membrane accepted the vibrations of the probe. In both of these cases therefore, according to the accepted interpretation, all mass motion was completely suppressed in the cochlear liquid, and both patients, according to Weber, should have been quite deaf. The air acuity curves taken with the other ear masked are shown in Fig. 4 and demonstrate almost identical sensitivity to air sounds throughout the entire range tested. Inasmuch as they should have been deaf to air vibrations according to the accepted interpretation and were not, the easy way to explain how they heard is to assume that it was by bone conduction. This makes it necessary to consider the hearing by bone conduction according to the accepted explanation of mass displacement in the cochlear liquid.

Von Bekesy, a prominent physicist who has been investigating problems of audition for many years, has presented the accepted interpretation for the hearing of bone-conducted sound in the form of three simple diagrams. Figure 5a shows a hypothetical cochlea in which the area of the bony wall related to the *scala vestibuli* and to the *scala tympani* is equal and where the two windows are equally yielding. The compression phase of the bone conduction sound contracts the capsule, and both windows are pushed outward through the increasing pressure in the liquid. Here there will be no relative displacement in the liquid. If, however, one window yielded more readily than the other, then the liquid would be displaced toward the more yielding membrane, and this would produce a movement in the basilar membrane as indicated in Fig. 5b. But if there were a greater area of bone applied to the *scala vestibuli* as indicated in the schematic

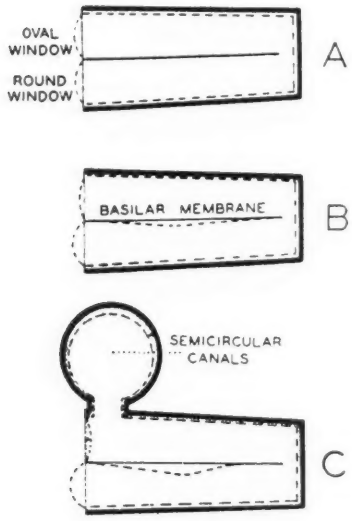

Fig. 5. The explanation for the hearing of bone conducted sounds according to von Bekesy (taken from Stevens and Davis).

semicircular canal and especially if the stapes were fixed, then the compensatory motions at the round window would be increased and the motional effect in the basilar membrane would be exaggerated as in Fig. 5c. It is unfortunate that when von Bekesy published this explanation he did not know of the experimental work by Kranz and myself on the sensitivity to bone-conducted sound. The von Bekesy interpretation is based on the accepted teaching that cases of stapes fixation enjoy a greater than normal sensitivity to bone-conducted sound. Our work demonstrated that the prolonged bone conduction described in cases of stapes fixation is not a fact. If anything, such patients hear bone-conducted sound somewhat less acutely than individuals with normal hearing.

Now let us see what results were obtained by the tests on bone sensitivity in Cases A and B. You will remember in Case A the stapes was demonstrated as fixed and in Case B both windows were movable, and that both had similar air acuity for all frequencies. According to the accepted interpretation Case A should have heard bone-conducted sound more acutely than Case B. Figure 6 shows the findings taken under conditions with the other ear masked. The curves clearly indicate that Case A was appreciably less sensitive to bone-conducted

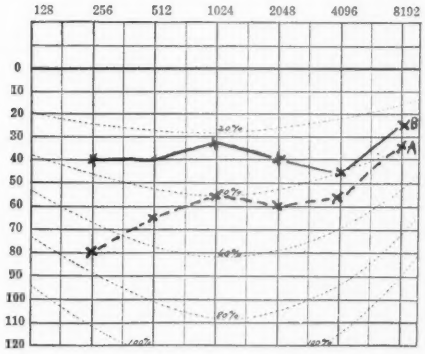

Fig. 6. Bone acuity in Cases A and B showing the disproportion in the sensitivity. Compare with the air acuity curves in Fig. 4.

sound than was Case B, when the reverse should have been true. It is also clear that if Case B was more sensitive to bone-conducted sound than Case A, then he was not hearing the air vibrations by bone conduction because the air sensitivity in the two cases was practically the same, especially for low tones.

There is one objection to this evidence. There is considerable variation in the sensitivity to both air- and bone-conducted sound especially in patients in whom the middle ear apparatus has been lost. The best evidence would be found in testing the same ear first with one window fixed and then with two windows movable. Fortunately, Lempert has furnished this information. The fenestration operation is performed on cases of stapes fixation, and these patients are carefully tested for air and bone acuity before and after the operation. According to the accepted interpretation cases of stapes fixation must be quite deaf to air-conducted sound unless they are hearing them by bone conduction. This was not supported by the evidence in Cases A and B.

In cases of stapes fixation mass displacements in the cochlear liquid due to an interaction between the two windows have been suppressed because one window is fixed. Lempert believes that "This fenestra is created in order to replace the non-functioning fenestra ovalis and thus to mobilize the labyrinthine perilymph and endolymph for air-borne sounds." This explanation is like that proposed by Can-

field and calls for some discussion because of the increasing importance of the fenestration operation in cases of otosclerosis. May I go back to the U-tube experiment? It was found that when one window was fixed no mass displacement in the water would come about, and all that would happen when pressure was exerted on the movable window was an increase in the pressure of the contained liquid. It was also indicated that if equal pressures were applied simultaneously to the two movable windows, a similar result would be obtained. The former condition may be likened to the behavior of the cochlear liquid when the stapes is fixed, while the latter condition is similar to creating a fenestra to replace the non-functional oval window. Theoretically, therefore, the fenestration operation would not mobilize the liquid because the sound pressures are applied to both windows at the same time, and according to the accepted interpretation no increase in the air acuity would be expected. Further, according to the accepted interpretation the described displacements of the labyrinth liquid toward the round window in cases of stapes fixation would be reduced through creating a second movable window related indirectly to the *scala vestibuli.* The fenestration operation should therefore, result in a decrease in bone sensitivity. Lempert, however, reports, "Improvement in hearing resulting from fenestration of the horizontal semicircular canal is improvement of air conduction only. Hearing by bone conduction is neither improved nor impaired by a successfully performed fenestration. It remains unchanged."

The accepted mass displacement in the cochlear liquid to be heard must take on the form of oscillations which are dependent not on the more movable window but on the more fixed one. The newly created fenestra may be more yielding than the round window membrane, but this will not produce a mobilization of the cochlear liquid. Obviously, the pressure in sound would be more readily transferred to the liquid through a thin diaphragm than through a thick one. This would suggest that the end organ reacts to the pulsating pressures in the liquid and not to the pulsating pressures on the auditory cells created by the assumed transverse vibrations in the basilar membrane.

In my opinion the results of the Lempert operation definitely prove that the Weber interpretation of a mass movement in the cochlear liquid as essential to audition is incorrect.

Mass displacement in the cochlear liquid, according to the accepted interpretation, may come about through an interaction between the dense otic capsule and the round window membrane.

Inasmuch as sound is a pendular displacement it follows that if the contraction in the bony capsule forces the liquid toward the yielding round window membrane, then pressure applied to the round window membrane will be adjusted in an expansion of the otic capsule. Just as the contraction of the larger area of the bony wall related to the *scala vestibuli* would tend to make the liquid drift toward the round window, so when the pressure is applied to the round window this same area would expand and permit the liquid to shift in the opposite direction. Accordingly, while air and bone vibrations, disregarding the speed of conduction from the source, are both operating normally in the same phase, the hearing of bone-conducted vibrations and of air-conducted vibrations by way of the round window should be in opposite phase in cases of stapes fixation. While von Bekesy believes that the displacement in the hearing of air vibrations is in opposite phase to the assumed normal reaction, under conditions of stapes fixation, he does not consider the possibility as outlined above but introduces a third way in which mass reactions in the cochlear liquid may come about. He holds that the *ductus endolymphaticus,* the *ductus perilymphaticus* and blood vessels act as compensation areas which permit the shifting of the labyrinth liquid when the pressure of the air vibrations is applied to the round window in the presence of a fixed stapes. The objections to this interpretation have been published and need not be discussed here. The essential difference between the Weber interpretation and that of von Bekesy in terms of otological experience is that according to the former the patients are deaf to air vibrations when the stapes is completely fixed, and according to the latter they become deaf to air vibrations before the stapes is fixed and after complete ankylosis a certain degree of air acuity returns. According to von Bekesy's interpretation the fenestration operation should reduce the sensitivity to the bone-conducted sound. Is it necessary to traduce the facts in an effort to explain the reactions in the ear to sound?

It was noted earlier in this paper that Weber's demonstration of a mass displacement in the cochlear liquid when the stapes of a specimen was pushed into the oval window may not be regarded as evidence that a similar reaction takes place to sound vibrations or even that it occurs during life. The physiologist, Kato, in 1913 made certain observations in his investigation on the function of the middle ear muscles. He found that when the tensor tympani was stimulated electrically to produce wide excursions of the drum membrane, no compensatory reactions could be detected at the round window so long as the stapedius was functional. However, when the

stapedius was incapacitated the contractions in the tensor tympani resulted in compensatory motions in the *membrana tympani secundaria*. These results appear to indicate that the leverage action of the ossicles operates as a shock absorber and that the function of the stapedius is to prevent the mass displacements demonstrated in the Weber experiment. Kato also found that his experimental animals exhibited reflex deafness to loud sounds in a much shorter time when the middle ear muscles were incapacitated than when the animals were normal. Luescher has demonstrated in the human being that the stapedius contracts to sound practically throughout the frequency range. The intensity required to elicit this reflex is about 60 db. The fact that Lurie found evidences of mass shifting in the cochlear liquid when an animal with incapacitated muscles was exposed to a sound intensity of 120 db., which is a million times greater than that required to produce the normal stapedial reflex, may not be considered as proof that this occurs normally.

Seventh, does the basilar membrane vibrate transversely to sound and does it have the function of a mechanical harmonic analyzer?

Obviously, if the mass displacements in the cochlear liquid have not been demonstrated as essential to audition, then the transverse vibrations in the basilar membrane which have been assumed to result by reason of these mass displacements are conjectural. It will be remembered that the function of the basilar membrane as a mechanical harmonic analyzer was based not only on the interaction between the two windows but also on a selective weighting which was dependent on the length of the columns of liquid in the two scalae. I will present three observations which oppose this. Patients in whom there is a *scala communis cochleae* exhibit a dehiscence which affords a connection between the *scala vestibuli* and the *scala tympani* proximal to the distal end of the cochlear duct. This means that the assumed mass shifting in the scalae does not reach the distal end of the basilar membrane, and no transverse vibrations in the part of the membrane would come about through an interaction between the two windows. According to the accepted interpretation these patients should be quite deaf to low frequency sounds. Polvogt and Crowe, however, have reported six cases of *scala communis cochleae* in which the hearing acuity was normal throughout the entire range tested.

A second observation may be made in relation to the selective tuning. If the site of the response in the basilar membrane is in part determined by the length of the columns of liquid applied to it in the scalae, then increasing the length of one of these columns

would move the site of reaction closer to the two windows. The patient then should hear all frequencies as of too high a pitch, and this condition should be quite characteristic of all cases with effusion into the middle ear. I am not aware that false hearing is characteristic in such cases.

The third observation is in relation to the fenestration operation. Creating a window in the lateral semicircular canal appreciably increases the length of the liquid column in the *scala vestibuli.* The assumed selective weighting would therefore shift the place of reactance in the basilar membrane nearer the two windows and should result in hearing all frequencies as of too high a pitch. This however, has never been reported. For these and for other reasons the accepted interpretation that the basilar membrane acts as a mechanical harmonic analyzer cannot be accepted.

Eighth, do the auditory cells act merely as signal stations with no specificity in response except to report the site of an acoustic disturbance in the basilar membrane?

The accepted interpretation assumes that the auditory cells are nonspecific in their reactions to the frequencies in sound vibrations and act merely as signal stations which report to the brain the pattern of the response in the basilar membrane. This assumption was based on the fact that the auditory cells from one to the other end of the organ of Corti all look alike, and therefore, must be similar in function. The situation reminds me of the identical twins who could be distinguished only by the mother. If she put her finger in Jim's mouth and he bit her, it was John. Structural similarity is not a criterion of functional similarity. If this were true then there could be no restriction in the fields of color vision, and it would be impossible to discriminate between the odor of garlic and that of roses.

The experimental evidence appears to confirm only three points in the accepted interpretation: first, that the drum membrane vibrates to the air sound heard; second, that the drum membrane vibrations are effectively conducted into the cochlea through the ossicle chain; third, that bone-conducted sound is heard in the same way as air-conducted sound. These three points were fairly well established in the Middle Ages. The acceptance of the Weber interpretation for 90 years may be construed as evidence of a respect justly due a great master, but it may not be regarded as evidence that his explanation was correct or even physically possible.

In closing may I be permitted to make assumptions? I am assuming that the auditory cells are specific in their reactions to the

frequencies in sound vibrations and that they are directly activated by the pulsating pressures applied to them through the labyrinth liquid. I am assuming that the anatomy of the apparatus may be correlated with a shock-absorbing function which protects the end organ against the mass displacements in the cochlear liquid. I am, therefore, in favor of having the motional reactions in the cochlea convincingly demonstrated before the differential equations set up to describe them are seriously considered. The evidence appears to indicate that while the conduction of sound vibrations to the auditory cells presents a simple problem in physics, the frequency analysis is dependent on a physiological reaction of which we know little or nothing. While there is no indication that much can be done to correct the physiological disability (perception deafness) we must not lose hope so far as the physical part of a hearing disability is concerned. Once we stop guessing and approach the problem in a scientific manner, perhaps more may be accomplished for the cases of conduction deafness.

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XXVI

EXPERIMENTAL SINUS SURGERY: EFFECTS OF OPERATIVE WINDOWS ON NORMAL SINUSES

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DULUTH

Some years ago I performed a series of experiments on dogs which showed the effect of removal of bands of mucous membrane from the frontal sinus. Certain facts were found which are here briefly reviewed.

It was found that, if bands of mucous membrane were removed from concave surfaces, elevated scars resulted which interfered more or less with the drainage of mucin as motivated by the ciliary mechanism. The degree of interference depended upon the elevation of the scar from the surface upon which it had formed and its position with reference to the stream of mucin. If the elevation were great and the scar sharp, and if it lay transversely across the direction of flow of mucin, it would act like a dam and would stop the flow and cause an accumulation of secretion behind it. If annular strips were removed completely around the entire circumference of the sinus, the resulting scars formed diaphragms. These diaphragms might be complete, or they might be incomplete with a central perforation through which the two portions of the sinus were connected. If the width of the desquamated band were sufficiently great, the diaphragm would be complete and impervious, dividing the sinus into two chambers, one of which had no outlet and was invariably filled with secretion.

If bands or areas of other shapes on flat surfaces were desquamated, the resulting scars were flat and seemed not to interfere seriously with the drainage mechanism.

When the entire sinus was desquamated, it tended to fill with scar and to become obliterated. Often cysts remained which were lined by active ciliated epithelium and filled with viscid translucent secretion. Sometimes the sinus reformed partially, making small irregular cavities spanned by scars. The cysts and reformed cavities probably resulted from portions of epithelium which had not been removed.

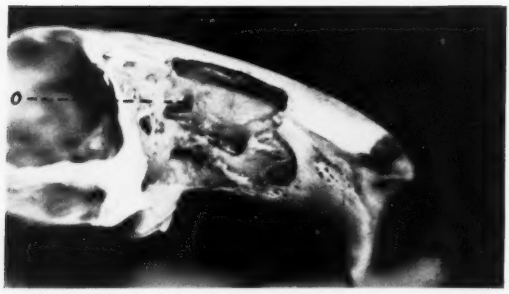

Fig. 1. Dissection of the right maxillary sinus in a rabbit's skull. The position of the ostium is indicated by "O".

Microscopic examination made on some of these scars since the results were published revealed that they were covered with well-ciliated epithelium (even thread-like strands which spanned from roof to floor were so covered) and that they were partially ossified. One may speculate upon the reason for the failure of the secretion to drain over these well-ciliated scars, and one may develop a number of theories to explain it, such as improper direction of ciliary action or division of the viscid secretion by the knife-like edge of the scar. In any case, whatever the explanation, the fact remains that these scars did obstruct drainage.

In all of these experiments the essential factor in the results seemed to be the laying down of white fibrous connective tissue in relatively avascular fields and the subsequent contracture of these scars.

The present study was made for the purpose of determining the effect, if any, of windows upon the drainage mechanism of normal sinuses. It was desired especially to study the effect of enlarging the ostium. Might windows also derange normal ciliary flow?

Material.—The maxillary sinus of the rabbit was used as subject for the experiments (Fig. 1). Eighteen sinuses were operated upon in these four experiments. Six of the sinuses served as controls. All of the animals were healthy at the beginning of the operations and remained so throughout the experiments. Two which became ill were discarded.

Technic.—All operations were performed under seconal anesthesia, administered intravenously, combined with a local injection

of 1% novocaine over the bridge of the nose. All operations in the four experiments were carried out with aseptic precautions such as are used in clinical surgery.

Operation.—The fur was shaved off the face and a mid-line incision made down the bridge of the nose through the skin and periosteum. The periosteum was stripped off over the sinus, and the roof of the sinus was opened. The bone of the roof and lateral wall was removed only widely enough to make a hole through which the intrasinus manipulations could be carried out. The windows at the ostium were made largely by means of a small currette under direct vision by breaking away the thin bony margins, after which the margins were trimmed with scissors, small punch forceps, or tiny rongeurs. The other windows were made with a small pair of scissors or a small knife aided by punch forceps. In most instances some care was taken to preserve enough epithelium to cover the bony margins of the operative window. However the walls of this sinus are so thin that there is little danger of subsequent closure of the windows, even when this precaution is omitted. At the end of the operation the skin incision was closed by interrupted silk sutures.

Controls.—It was necessary to control especially two factors in these experiments: first, the effect of the surgical approach through the roof of the sinus; second, the possibility of infection accidentally introduced during the operation as being the cause of the suppurative sinusitis which developed in some instances.

In order to test these two factors six normal sinuses were opened through the roof and lateral wall as described, except that no aseptic precautions were taken. No sterile drapes were used, the field of operation was neither shaved nor sterilized, and neither the surgeon's hands nor his instruments were sterilized. In addition, certain physiology experiments involving intrasinus manipulations were carried out with non-sterile implements. Care was taken, however, not to damage the lining of the sinus, especially near the ostium. In closing the wounds the incision was stitched with silk thread. No dressing was applied. Results: all six sinuses healed without any sign of infection or other disturbance, thus showing that the surgical approach did not seriously injure the sinus and that accidental infection introduced at the time of the operation was not the cause of suppuration which occurred in the experiments to be described.

Ciliary Drainage.—The plan of the flow of mucus within the maxillary sinus of the rabbit was tested with India ink. The approximate result is given in Fig. 2. As has been experienced before,

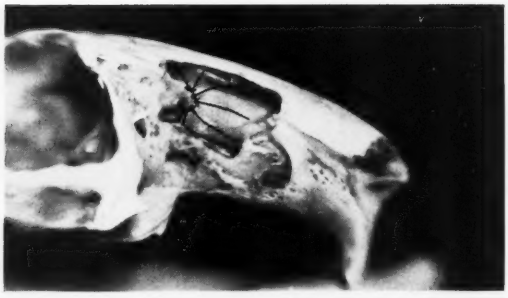

Fig. 2. Approximate plan of ciliary drainage in the maxillary sinus of the rabbit.

the testing of ciliary action under intravenous anesthesia from barbiturates is not very satisfactory. It is difficult to obtain well defined movement.

Experiment 1.—Enlargement of the ostium. The ostium was enlarged to form a large window between the right maxillary sinus and the nasal cavity in three rabbits, "C", "E" and "H" (Fig. 3). These three sinuses were all normal when operated upon. After operation all three promptly developed a suppurative sinusitis with some drainage from the right nostril and a large abscess on the bridge of the nose (Fig. 5). At first it was thought that the opening made must have closed up, but this was not the case. At necropsy the window was found to be widely patent in all three (Fig. 4).

Protocols.—"C". 2/27/39. Operation on the right maxillary sinus was performed as described above under seconal anesthesia. The sinus was found to be normal. The ostium was curretted in such a way as to make a large window into the nasal cavity.

10th day. There was a large, inflamed swelling on the bridge of the nose.

12th day. Pus was coming from the swelling.

22nd day. The right maxillary sinus was reopened and inspected. There was a large abscess on the bridge of the nose, and the sinus was found to be full of pus and the mucous membrane found to be inflamed.

115th day. The rabbit was sacrificed. Necropsy revealed thickened bone over the right maxillary sinus; the sinus was filled with

Fig. 3. Position of the operative window in Experiment I. In this experiment the window included the ostium.

Fig. 4. Specimen skull from Experiment I. The horse-hair probe passes through the operative window. The windows in all three of the animals in this experiment remained widely patent, but all three developed suppurative sinusitis.

Fig. 5. Rabbit "H" showing the abscess which developed on the bridge of the nose following enlargement of the ostium of the right maxillary sinus. The skull from this animal is pictured in Fig. 4.

pus; the mucous membrane was inflamed, but the enlarged ostium was widely patent and communicated with the nasal cavity.

"H". 2/27/39. The right maxillary sinus was opened and found to be normal. The ostium was enlarged by means of a currette.

12th day. There was a large inflamed swelling on the bridge of the nose which exuded pus through the stitch holes.

18th day. The right maxillary sinus was reopened and inspected. There was a large abscess on the bridge of the nose, and the right maxillary sinus was found to be full of pus. The bone over the sinus was thickened, and the mucous membrane was inflamed and thickened. The artificial window at the ostium was widely patent.

115th day. The rabbit was sacrificed. At necropsy the bone over the right maxillary sinus was found to be thickened, the lining mucous membrane was thickened, and the cavity somewhat reduced in size. The cavity was empty and clean, however, the sinusitis having healed since the operation of exploration (Fig. 4).

"E". 3/1/39. The right maxillary sinus was opened and found to be normal. The ostium was enlarged by means of a currette, making a large window into the nasal cavity.

8th day. There was a large inflamed swelling on the bridge of the nose.

17th day. The right maxillary sinus was reopened and inspected. There was a large abscess on the bridge of the nose which was draining through a fistula. The sinus was found to be filled with pus. The window at the ostium was patent but was surrounded by granulations.

113th day. The rabbit was sacrificed and necropsy was performed. The right maxillary sinus was found to be much reduced in size and full of pus. The window at the ostium was patent.

Experiment II.—Window through the lower medial wall and floor. An artificial window was made through the floor and lower medial wall between the right maxillary sinus and the nasal cavity in three rabbits, "I", "M", and "Q" (Fig. 6). These three sinuses were all normal when operated upon. Following operation two rabbits—"I" and "Q"—developed a suppurative sinusitis. The sinus in the third was clean when examined and appeared to be normal, except that there was a little mucus in the lower anterior recess just in front of the artificial window. These animals did not develop the large abscess on the bridge of the nose as did those in Experiment I.

Protocols.—"I". 2/6/40. The right maxillary sinus was exposed and found to be normal. A large window was made through the lower medial wall and floor by means of a punch forcep. This opened directly into the nasal cavity.

20th day. The wound on the bridge of the nose appeared to be open, but it was not draining.

34th day. The animal was sacrificed. At necropsy the right maxillary sinus was found to be full of pus and the mucous membrane thickened and inflamed. The operative window was widely patent (Fig. 7).

"M". 7/27/39. The right maxillary sinus was opened and found to be normal. A large window 7½ mm. in diameter was made through the floor and lower medial wall.

62nd day. The animal was sacrificed and examined. The right maxillary sinus was found to be empty and clean with the exception of a very small amount of mucin in the lower anterior recess just at the anterior margin of the window. The window was widely patent.

"Q". 2/6/40. The right maxillary sinus was unroofed and found to be normal. An artificial window was made through the floor and lower medial wall. The window was outlined by means of a cataract knife and the bone and mucous membrane bitten away

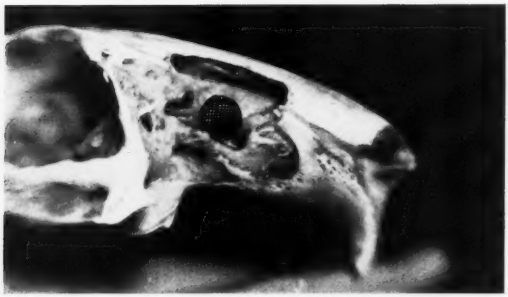

Fig. 6. Position of the window in Experiment II.

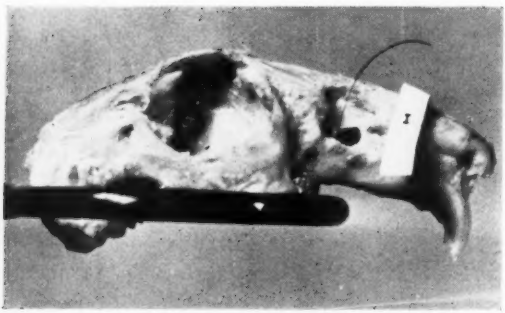

Fig. 7. Specimen skull from Experiment II. The horse-hair probe passes through the operative window. The operative windows remained patent in all three of the animals used, but two, "I" and "Q", developed suppurative sinusitis.

with punch forceps. In addition, certain transplants of epithelium were made which are to be described subsequently.

35th day. The animal was sacrificed and examined. The right maxillary sinus was found to be filled with pus, and the mucous membrane was inflamed. The artificial window was patent but opened into another sinus instead of into the nasal cavity. This sinus also was found to contain pus.

Experiment III.—Window high up on medial wall. A window was made through the medial sinus wall opening into the nasal cavity just under the bridge of the nose in the right maxillary sinus of three rabbits, "K", "X", and "Z" (Fig. 8). These three sinuses were all normal when operated upon. One, "K", developed suppurative sinusitis following operation, as found at subsequent operation of exploration, and two, "X" and "Z", remained normal.

Protocols. "K". 7 20 39. The right maxillary sinus was exposed and found to be normal. The opening through the roof was extended medially on the bridge of the nose in order to expose the nasal cavity. A triangular window which measured 6 mm. on each side was made in the wall between the sinus and the common nasal meatus just under the bridge. The apex of this triangular window was directed inferiorly.

65th day. The animal was sacrificed. At necropsy the artificial window was found to be widely patent, but the maxillary sinus was filled with thick cheesy pus, as was also the next sinus immediately underlying (this sinus drains through the maxillary) and the right nasal space (Fig. 9).

"X". 11 18 40. The right maxillary sinus was exposed and found to be normal. A window was made high up on the medial wall between the sinus and the common meatus. Inadvertently the window was placed somewhat farther anteriorly on the medial wall than the mid-point.

17th day. The right maxillary sinus was reopened and inspected. The operative window was widely patent and the sinus clean, empty, and normal in appearance.

"Z". 12 5 40. The right maxillary sinus was exposed and found to be normal. A window was made high up on the medial wall between the sinus and the nasal cavity, extending between the roof and the mid-point of the sinus in a vertical direction. A small

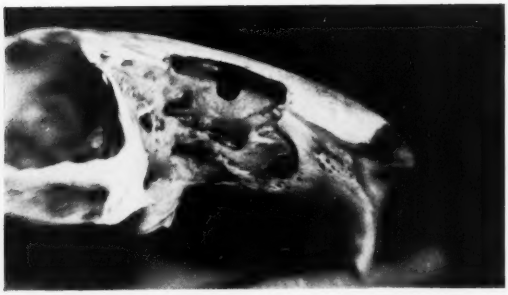

Fig. 8. Position of the window in Experiment III.

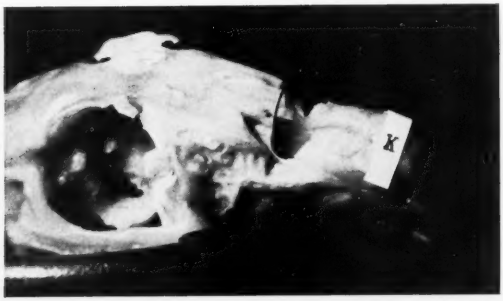

Fig. 9. Specimen skull from Experiment III. The horse-hair probe passes through the operative window. Of the three animals used in this experiment one, "K", developed suppurative sinusitis. The windows remained widely patent in all.

part of the adjacent turbinate was removed from the region of the posterior margin of this window.*

15th day. The right maxillary sinus was reopened and inspected. The operative window was widely patent and measured 6 x 6 mm. The sinus was clean, empty, and normal in appearance.

Experiment IV.—Window in the anterior recess. A window was made in the anterior upper portion of three maxillary sinuses in two rabbits, "L" and "ZZ", at a point as far from the ostium as it was possible to go (Fig. 10). The right maxillary sinus was operated upon in "L", and both in "ZZ". These three sinuses were all normal when operated upon. All three healed without any complications, and at subsequent operation of exploration all three were found to be empty and clean, and all three windows were widely patent.

Protocols.—"L". 7/27/39. The right maxillary sinus was opened through the roof and found to be normal. The ciliary flow was tested and found to be approximately according to the plan sketched in Fig. 2. A window was made between the sinus and the nasal cavity by resecting the anterior superior recess, which bulges more or less into the nasal cavity in the form of a bulbous protuberance.

62nd day. The animal was sacrificed. Both maxillary sinuses were opened and examined. Both were empty and normal. The operative window in the right was widely patent (Fig. 11). Both nasal cavities were also clean.

"ZZ". 12/5/40. Both maxillary sinuses were opened and found to be normal. A window was made in the anterior upper recess of both as far as possible from the ostium. This window opened directly into the common meatus.

15th day. The external wound was nicely healed. Both sinuses were exposed and reopened, and both were found to be clean, empty, and normal in appearance. The operative window in both was widely patent.

*Two other animals, "P" and "O", were operated upon on the same day and were sacrificed on the same day. The operations in both were the same. The right maxillary in each was exposed and a window made through the medial wall as in Fig. 6. At the operation of exploration performed some weeks later the right maxillary in both showed suppurative sinusitis, although the window was patent in both. At necropsy (9/23/40) four months later the window was again found to be patent in both with sinusitis still persisting in "O", but it had healed in "P".

Unfortunately the laboratory cards bearing the dates of the first two operations were lost. For that reason these animals were omitted.

Fig. 10. Position of the window in Experiment IV.

Fig. 11. Specimen skull from Experiment IV. The probe passes through the operative window. None of the sinuses in this experiment developed sinusitis. The windows in all three remained patent.

COMMENT

These experiments show that operative windows made between the maxillary sinus and the nasal cavity in rabbits result in suppurative sinusitis under certain circumstances, even though the sinuses be normal when the windows are made. The result seems rather definitely to depend upon the position of the window with reference to the ciliary mechanism. That the suppuration might be due to the operative approach to the sinus or to the outside infection accidentally introduced at the time of operation was ruled out by the control series described in the introduction. The experiments indicate that windows made at or near the ostium interfere so seriously with the normal sinus physiology that the sinus becomes infected as a result. On the other hand, if the windows are made at points distant from the ostium, suppurative sinusitis is not so apt to occur. This is to be expected since the ciliary streams from the entire cavity converge at and about the ostium, and damage there would be more serious in its effect than at points farthest from the ostium. Windows made in intermediate positions sometimes caused suppuration and sometimes did not.

Summarizing these experiments, we find that in the 12 sinuses operated upon the operative window remained open in all. Six of the 12 became infected. (Including the two on which the records were lost, eight of 14 became infected.) All three of those in which the window was made at the ostium promptly developed suppurative sinusitis. None of the three in which the window was made as far as possible from the ostium became infected postoperatively. Of the three in which the window was placed in an intermediate position low down on the medial wall two became infected, and one did not. Of the three in which the window was placed high on the medial wall one became infected, and two did not. (Again including the two in which records were lost, three out of five in this position became infected.)

These experiments show that the maxillary sinus in rabbits will not tolerate operative procedures at or near the ostium, whereas they are tolerated fairly well if made at a distance from the ostium. The proportion of those operated upon in which suppuration results might be different in a larger series. It would have been better for the purposes of this study if there had been 25 sinuses in each of the four groups, but with the limited facilities available this was not practicable. It would also be of help to know the incidence of spontaneous sinusitis in rabbits. Six spontaneously infected sinuses were found in other apparently healthy rabbits while doing these experiments.

When a rabbit becomes ill and debilitated, it seems prone to develop rhinitis and sinusitis.

It is of interest that wide open windows, as well as obstructing scars, can interfere with the ciliary mechanism. The *modus operandi* is probably through a break in the continuity of the ciliary mechanism.

It cannot be concluded from these experiments that exactly the same results would occur in the sinuses of other species or in man. The dog, for instance, does not develop suppurative sinusitis readily even in the presence of complete stasis of sinus secretion. I think, however, that it can be fairly inferred that the region of the ostium is a vital part of the physiological mechanism of a sinus and that it cannot be mutilated with impunity. This should be taken into account in clinical surgery.

It cannot be concluded from these experiments that windows which are made far from the ostium would be effective in curing sinusitis. These experiments deal only with the relation of operative windows to normal sinus physiology. How effective harmless windows may be in a curative way is another story.

CONCLUSIONS

1. Rabbits develop suppurative sinusitis readily as a result of operative windows made between the maxillary sinus and the nasal cavity.

2. Sinusitis is much more apt to occur if the window is made at or near the ostium than if it is made at a point distant from the ostium.

3. Obviously a sinus may not be mutilated surgically with impunity in disregard of the physiology of the ciliary mechanism.

4. Apparently open windows, like scars, may disrupt sinus drainage if placed in positions where they interfere with ciliary flow.

5. It is possible to make windows in such positions with reference to the ciliary mechanism that they do not seriously interfere with drainage.

I am indebted to Dr. D. L. Tilderquist and to Miss Caroline Marshall for financial grants and to Miss Margaret Helquist for technical assistance in this work.

Thanks are also due to Eli Lilly and Company for supplying the anesthetic used in these experiments.

626 MEDICAL ARTS BLDG.

XXVII

TRANSITIONAL CELL CARCINOMA OF THE UPPER RESPIRATORY TRACT*

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MAURICE LEV, M.D.
AND
MARGERY BLAHD, M.D.

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There is considerable confusion in the literature as to the nomenclature and biologic nature of malignant tumors of the upper respiratory tract. In general it has been recognized that there are at least two types of such tumors. These two types differ only in whether or not the cells have a tendency to mimic the normal metamorphosis of cell types in stratified squamous epithelium. Those tumors whose cells have this tendency have been variously called: squamous cell carcinoma, spinous cell carcinoma, epidermoid carcinoma of the skin or mucous membrane type, and various other names. The other group includes anepidermoid carcinoma, transitional cell carcinoma, anaplastic carcinoma, carcinoma solidum simplex, basal cell carcinoma, lymphoepithelioma, etc.

It is the purpose of this paper to attempt to clarify tumors of the latter variety—the "non-squamous" or the "non-spinous" type. This will be done by an analysis of such tumors, (a) historically, (b) morphologically, and (c) prognostically.

HISTORICAL RETROSPECT

For many years, tumors of the upper respiratory tract have been noted which consisted of cells more or less resembling the basal or slightly more superficial layer of stratified squamous epithelium with little or no tendency towards cornification. Krompecher[1] maintained that these tumors were derived from the multiplication of the cells of the basal cell layer which retained their basal cell character-

*Aided by a grant from the Gusta Rothschild Fund.

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istics. He therefore called them basal cell carcinomas, which, however, differed from those of the skin by being more malignant. He later suggested that they be called basaliomas.[2] Broders[3] called them basal cell-like carcinomas, as they varied somewhat from the morphology of the basal cell carcinoma of the skin, and metastasized in contrast to the latter. Crowe and Baylor[4] reported a series of nasopharyngeal carcinomas which differed in their morphology from the usual squamous cell type. In 1927 Quick and Cutler[5] presented a series of nasopharyngeal and laryngeal tumors which differed both clinically and morphologically from the "squamous" variety. These tumors occurred in the tonsil, base of tongue, and larynx, and were clinically highly malignant. In the majority of cases the first sign was regional lymphadenopathy, and there was a tendency toward distant metastasis. They responded excellently to radiation. Histologically the tumor consisted of solid groups or anastamosing columns of closely packed, small, polyhedral cells with hyperchromatic nuclei and scant cytoplasm, with no spines or tendency toward pearl formation. These tumors were called transitional cell carcinomas. They were considered to have originated either in the transitional epithelium found in the nares, accessory sinuses, crypts of the tonsils, portions of the larynx and ducts of the mucous glands or in the deep layers of the stratified squamous epithelium or in misplaced embryonal tissue. Ewing[6, 7, 8] likewise grouped certain tumors together as transitional cell carcinomas. Such tumors are found in the urinary bladder, upper respiratory tract and cervix. They occur in regions covered by both transitional and stratified squamous epithelium and are characterized by more rapid growth, greater malignancy and greater radio-sensitivity than squamous cell carcinomas of the same region. They are alleged to be derived either from basal or squamous cells.

Despite the introduction of the term transitional cell carcinoma for some of these "non-squamous" cell carcinomas, uniformity of nomenclature did not follow. The French scientists called these tumors anepidermoid, the Germans, carcinoma simplex; some used the term undifferentiated carcinoma, embryonal carcinoma, and a few, transitional cell carcinoma. Still others denied the epithelial origin of these tumors and called them lymphosarcomas. Schinz and Baumann-Schencker[9] adopted the term transitional cell carcinoma for 29 such tumors. They pointed out that the morphology of the tumor varied according to the part of the tumor from which the section was taken. Thus in peripheral sections the cells were arranged in palisade formation with flattened nuclei, while in central sections

the cells were round or polyhedral with round or oval nuclei containing fine, delicate, and deeply staining chromatin material, and weakly basophilic cytoplasm.

The confusion concerning the so-called transitional cell carcinoma has been further accentuated by the question of the nature of the so-called lymphoepithelioma. In 1921 Schmincke[10] described tumors of the nasopharynx consisting of irregular anastamosing trabeculae of ill-defined cells with large vesicular nuclei—apparently epithelial cells, in combination with a large number of lymphocytes. Reverchon and Coutard[11] in the same year reported from Regaud's Clinic a somewhat similar tumor in which, however, the component cells seemed to possess intercellular bridges thus producing a protoplasmic syncytium embedded in varying numbers of lymphocytes. Because of the presence of these two elements, epithelium and lymphoid tissue, these tumors were called lymphoepithelioma. This was based on the conception that lymphoepithelium is a distinct type of epithelium found in the pharynx, thymus and ileum.[12] These tumors have been found in the nasopharynx, tonsils, and thymus, and less frequently in the hypopharynx, but none have been reported in the ileum. Capell[13] and Jovin[14, 15] attempted to show that the Schmincke and Regaud types were closely related. The tumors were supposed to differ from reticulum cell sarcoma by the relative sparseness of reticulum fibers. In spite of this, however, Edling,[16] Zalka[17] and Oberling[18] felt that these tumors were undifferentiated reticulum cell sarcomas. Fitzhugh[19] in 1938 collected 150 lymphoepitheliomas from the literature.

The relationship between transitional cell carcinoma and lymphoepithelioma was discussed by Tobeck,[20] who questioned the existence of a lymphoepithelioma and suggested that this was a transitional cell carcinoma secondarily invaded by lymphocytes. Harvey, Dawson and Innes[21] considered that so-called lymphoepitheliomas were in some cases transitional cell carcinomas and in others reticulum cell sarcomas. Zuppinger[22] included both tumors under the non-committal term carcinoma of the lymphoepithelial group. Jovin[15] and Lacassagne,[23] however, felt that transitional cell carcinoma is a type of lymphoepithelioma. Ewing[7, 8] pointed out the difficulties involved in differentiating these two types of tumor.

Under the term spindle cell carcinoma, Martin and Stewart[24] included certain tumors of the larynx and other organs. The characteristic cells of these tumors were fusiform or spindle-shaped, lying usually in an increased amount of connective tissue. Under the term

carcinosarcoma of the larynx, five cases have been reported.[25] Baker and Lambert[26] reported a tumor of the vocal cord histologically diagnosed as polymorphic prickle cell carcinoma with spindle and giant cell formation. Frank and Lev[25] in a study of carcinosarcoma of the larynx felt that these were squamous or transitional cell carcinomas which had undergone morphologic variations.

Thus, we see from this review that the subject of "non-squamous", anepidermoid or transitional cell carcinoma is in a state of confusion. In an attempt to clarify this problem, all the epithelial tumors of the upper respiratory tract seen in the pathological laboratory of the Michael Reese Hospital in the last ten years which were diagnosed as being other than squamous cell carcinomas were restudied morphologically and clinically. In some instances only biopsies were available, and in others, larger sections or whole tumors were studied. These tumors were then compared with the squamous cell carcinomas, both from the standpoint of morphology and prognosis.*

HISTOLOGIC APPEARANCE OF TRANSITIONAL CELL CARCINOMA

In order to be able to differentiate the non-squamous cell variety, we had to demarcate definitely the squamous or spinous cell type. The fundamental cell here was a polygonal, relatively large cell with sharp cell borders, round or oval, relatively pale nuclei with sharp nuclear membranes, usually prominent nucleoli, and a copious amount of cytoplasm with varying intensity of eosinophilic staining. These cells may or may not have had a tendency towards cornification, and they may or may not have had a tendency towards arrangement in "sarcomatous" formation.[25] Any tumor presenting any such cells was considered to be a squamous cell carcinoma or at least to possess squamous cell characteristics and thus was eliminated from the group under question.

Among the tumors which did not show the squamous cell tumor characteristics, the following types could be differentiated:

Type I—a small basal cell type. Here the component cell was a small, oval, fusiform, spindle-shaped or irregularly shaped cell. These cells were arranged in cords or masses. The nuclei filled most of the cells and were round, oval, fusiform or spindle shaped, and markedly hyperchromatic. The cytoplasm was scant, faintly basophilic or bluish-pink. The cells had a tendency towards arrangement in whorls, which was most marked in the antral carcinomas. The

*We are indebted to Drs. J. C. Beck, M. Cutler, S. J. Pearlman, S. Salinger and E. Uhlmann for the clinical records of their respective patients.

cells showed moderate to marked difference in size and shape, with a moderate number of mitotic figures. Two such tumors of the small basal cell variety were noted, one in the tongue and one in the antrum.

Type II—a medium sized basal cell type. Here the component cell was larger than the former or equal in size to a small basal cell. It was cylindrical, fusiform, or spindle shaped. The nucleus was relatively large, oval, fusiform, or spindle shaped, and markedly hyperchromatic. The cytoplasm was relatively scant, although more copious than in the previous type, faintly basophilic or bluish-pink. In some there was a tendency towards a whorled arrangement of cells. The difference in size and shape was in some tumors moderate and in others marked. The number of mitotic figures varied from small to moderate, but in general they were less numerous than would be indicated in the presence of the degree of variation in the size and shape of the tumor cells. Such tumors were found in the mouth (one), antrum (one), pharynx (two), and larynx (five). The cells of these tumors, more than of the others, resembled in their shape and arrangement those of the basal cell carcinomas of the skin. They presented, however, a greater variation in size and shape.

Type III—a large basal cell type. Here the component cells equalled or exceeded in size the cylindrical basal cell. The tumor consisted of large cylindrical, fusiform, or spindle shaped cells with oval, fusiform or spindle shaped nuclei which were only slightly hyperchromatic. The nucleus, although large, occupied less space in the cell in comparison to the above mentioned types. The cytoplasm was moderate in amount and bluish-pink. The difference in size and shape was generally moderate but sometimes marked. The number of mitotic figures in some cases paralleled the degree of difference in size and shape but often exceeded it. The tumor cells in some instances showed a plexiform arrangement, resembling that of connective tissue tumors. Such tumors were found in the mouth, one; tongue, one; palate, one; antrum, two; pharynx, two; tonsil, two; and larynx, three.

Type IV—tumors arising in the mucous membrane of the nose differing histologically from the above mentioned types. These tumors consisted of masses of anastamosing cords of small polygonal cells which on superficial examination resembled those seen in certain reticulum cell sarcomas. The nuclei occupied a greater part of the cell body, were round or slightly oval, and had a distinct nuclear membrane with well-stained, punctate chromatin material. These

nuclei were not as hyperchromatic as those of the small basal cell type. The cytoplasm was small in amount, slightly basophilic or bluish-pink. There was a moderate to marked variation in size and shape with few or many mitotic figures. The number of mitotic figures was either more or less numerous than would be indicated in the presence of the degree of variation in the size and shape of the tumor cells. Four such tumors were seen.

Type V—a separate type of carcinoma noted in the pharynx. This consisted of a mass of moderately large cells, with indistinct cell borders. In some regions the cells were closely approximated, simulating epithelium. In others they were loosely arranged and resembled reticulum cells. The nuclei were pale and round or oval. The cytoplasm was moderate in amount and bluish-pink. There was marked difference in size and shape of the cells, and numerous mitotic figures were noted. A scattering of lymphocytes was present throughout. This tumor belongs to the variety described as lymphoepithelioma.

Type VI—still another type of carcinoma noted in all regions of the upper respiratory tract. These tumors consisted of irregular masses of cells which appeared to be a cross between the basal and spinous cells. The nuclei were large, round or oval and moderately hyperchromatic. The cytoplasm was abundant and slightly basophilic. The difference in size and shape was generally marked. The number of mitotic figures varied from few to many, but again they were less numerous than would be indicated in the presence of marked variation in the size and shape of the tumor cells. These cells seemed to be atypical basal cells. However, that they might be atypical squamous cells could not be ruled out. These tumors were found in the tongue, one; antrum, one; pharynx, two; oral cavity, one; and larynx, four. They differed morphologically from those to be mentioned below as squamous cell carcinomas with transitional cell features or vice versa. The latter actually showed two different types of cell, some being squamous and some transitional. In contradistinction to these, the tumors in this group (6) consisted of cells each of which resembled in part the transitional cell and in part the squamous cell.

Type VII—a tumor encountered in the larynx and in the tonsil, the cells of which did not conform to any one type of cell. The variation in size and shape of the cells was very conspicuous and there were numerous mitotic figures.

DISCUSSION

A study of the first three types of tumor reveals them to have certain common features: (1) The nuclei are hyperchromatic; (2) the cytoplasm is relatively scant; (3) there is a tendency towards cylindrical or fusiform shape; and (4) there is a tendency towards a whorled arrangement of the cells, at times suggestive of sarcoma. The first three features show their resemblance to the normal basal cell or to the cells of any of the layers of pseudo-stratified columnar cells. Although they bear some resemblance to the cells of the layers immediately adjacent to the basal layer of stratified squamous epithelium, the latter tend to be less hyperchromatic and to have more of a polygonal shape than the cells of these tumors. They bear no similarity to the true squamous or spinous cell.

If it is true, as Mekie[27] indicated, that all the layers above the basal layer of stratified squamous epithelium are degenerated forms of the basal cells, then it would be difficult to conceive of tumors arising from any but the basal layer. If we add to this the resemblance of the tumor cells to the basal cells, one is justified in considering these tumors which are present in regions covered by stratified squamous epithelium as derived from basal cells which have retained their basal characteristics. The difference in the size of these cells can be accounted for by the difference in size of the normal basal cells in various locations, in addition to morphological alterations dependent upon the environment of the tumor cells (Frank and Lev[25]). That this is very likely so is seen in several tumors which have cells of both the large and small basal cell variety. When the tumor arises from pseudo-stratified columnar (transitional) epithelium, then the tumor may take origin from any of the cells.

As far as the nasal carcinomas are concerned, their component cells bear strong similarity to the cells of the Schneiderian membrane. This membrane consists of pesudo-stratified ciliated columnar or simply ciliated columnar epithelium. It is thus closely related to transitional epithelium. The columnar cells may be very low, almost cuboidal. Thus these nasal tumors may be considered to be in the same category as Types I to III.

The nomenclature of these tumors is clear when they arise from pseudo-stratified ciliated columnar epithelium. The term "transitional cell carcinoma" is justified in this case but is confusing when the tumors arise in the region of stratified squamous epithelium. For the assumption then is that the tumor arises either (1) from the cell layer adjacent to the basal cell (transitional layer); (2) from the

ducts of mucous glands; or (3) from misplaced embryonal tissue. In our opinion it is not likely that the first contention is valid. For when we leave the basal layer, the potentialities of the cells is towards the squamous variety and cornification. Thus, all such tumors should show some squamous cell carcinoma characteristics. Of course it is possible that the tumors may arise from the ducts of mucous glands or from embryonal tissue.

Such terms as basal cell carcinoma or basalioma seem justified since, as mentioned above, there is a strong possibility that the tumors arise from the basal layer of stratified squamous epithelium. When the tumor arises in the region of pseudo-stratified ciliated columnar epithelium, these terms would still seem valid. There are, however, certain objections to the term basal cell carcinoma. As now applied to certain tumors of the skin, the term connotes a relatively benign tumor both morphologically and clinically. This is not true of the above mentioned tumors. Furthermore, Krompecher[1, 2] used the term for certain tumors of the breast, prostate, and other organs, and thus the term would lead to a grouping together of dissimilar tumors of the upper respiratory tract, breast, prostate, etc. As for the term basalioma, it has the added objection of not including the epitheton carcinoma.

In the absence of any fitting term for these tumors, and in order not to clutter up the literature further with new terminology, we are applying the term transitional cell carcinoma to these tumors. This term is synonymous with basal cell carcinoma arising from mucous membranes, with basalioma, carcinoma simplex, undifferentiated carcinoma, and anepidermoid carcinoma in the upper respiratory tract.

As far as Type V is concerned, this is the tumor called in the literature lymphoepithelioma of the Regaud-Jovin type. The absence of any marked reticulum formation speaks against reticulum cell sarcoma. The cells are apparently epithelial but resemble neither the basal nor the squamous cells. The question as to whether the lymphocytes are an integral part of the tumor cannot be answered here. From the morphologic standpoint one is inclined to separate this tumor from the remainder as an atypical carcinoma. However, to consider this atypical type of tumor as the basic type, and the transitional cell carcinoma as modifications of this type, as Jovin[15] has done, is not justified morphologically.

As far as Types VI and VII are concerned, these are probably variations of the transitional or squamous cell types. In one case,

several biopsies of the same tumor revealed a large basal cell type of transitional cell carcinoma, a crossed basal-squamous type and an atypical type. In another instance several biopsies revealed a crossed basal-squamous cell type, an atypical type and a transitional cell carcinoma with squamous cell features. One cannot exclude the possibility that some of the cell variations may have been the result of radiation therapy.

We may now reclassify malignant tumors of epithelial origin arising in stratified squamous, pseudo-stratified ciliated columnar, or ciliated columnar epithelium (Schneiderian membrane) as follows:

1. Squamous cell carcinoma. The cell type here is a large, more or less polygonal cell with a sharp cell outline. The nucleus is large, round or oval with a distinct cell membrane. The chromatin material is coarse and not very deeply stained, but there is a distinct, prominent nucleolus. The cytoplasm is abundant with varying degrees of eosinophilic staining. The nuclear-cytoplasmic ratio is relatively low. There may or may not be a tendency towards pearl formation.

In our opinion, it is inadvisable to call these tumors squamous cell carcinomas because the term implies an origin from squamous cells, which are either degenerating or dead. However, since this expression is so widely used, it might be confusing to discard it in favor of the more appropriate term, spinous cell carcinoma. Therefore we will use the accepted nomenclature.

2. Transitional cell carcinoma. Here the cell type is a cylindrical, fusiform, spindle or occasionally cuboidal cell with a not very sharply demarcated cell membrane. The size of the cell varies from a size somewhat larger than a monocyte to that larger than a normal basal cell. The nucleus is relatively large, fusiform or spindle shaped, but occasionally round or oval. It is distinctly hyperchromatic. The cytoplasm is relatively scant with a tendency towards basophilic staining. The nuclear-cytoplasmic ratio is high. There may be a tendency towards sarcoma-like arrangement.

3. Squamous cell carcinoma with transitional cell features, and transitional cell carcinoma with squamous cell features (combination types). Combinations of squamous cell carcinomas and transitional cell carcinomas are more common than transitional cell carcinomas alone, although less common than pure squamous cell carcinomas in the upper respiratory tract. It is possible that most tumors would be found to have characteristics of both if they could be sectioned completely. This is borne out by the fact that several biopsies of the

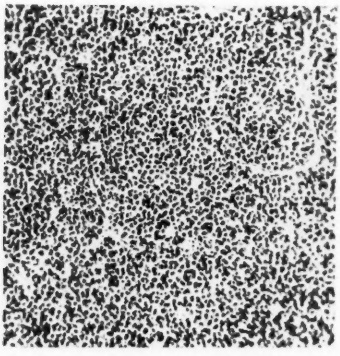

Fig. 1. Carcinoma arising in the mucous membrane of the nose. Note the resemblance of this tumor to a reticulum cell sarcoma. (Hematoxylin eosin preparation X130.)

same tumor in this series revealed transitional cell carcinoma once and once squamous cell carcinoma.

4. Atypical carcinoma. Here are included the so-called lymphoepithelioma of the Regaud-Jovin and Schmincke types, also those tumors whose cells have characteristics of both the squamous and basal cell types, and those generally bizarre anaplastic carcinomas whose cell type cannot be included elsewhere.

Adenocarcinomas, which also occur in the upper respiratory tract, do not fall within the scope of this study.

Transitional cell carcinomas which originate in stratified squamous epithelium may be considered as rising from the multiplication of the cells of the basal layer. In the normal growth and development of basal cells, some are destined to assume the role of the parent basal cell, while others proceed on towards cornification. Transitional cell carcinomas are most likely derived from the multiplication of those basal cells which retain their potentialities as basal cells. Squamous cell carcinomas on the other hand are most likely derived from the multiplication of those basal cells which go on towards cornification. In view of their common origin and the fact that all basal cells apparently contain some potentialities for cornification, it is not surprising that many tumors show the characteristics of both transitional and squamous cell carcinomas.

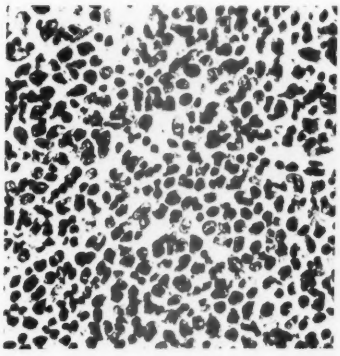

Fig. 2. Carcinoma arising in the mucous membrane of the nose. Higher magnification of similar field as shown in Fig. 1. (Hematoxylin eosin preparation X280.)

Where malignant tumors arise from pseudo-stratified ciliated columnar, or simple ciliated columnar epithelium, they will usually be transitional cell carcinomas. There is a marked similarity between these cells of columnar epithelium and the cells of the basal layer of stratified squamous epithelium. Therefore, tumors derived from pseudo-stratified or simple columnar epithelium cannot be differentiated from those arising from the basal layer of stratified squamous epithelium, although there may be a tendency towards whorl formation in the former.

PROGNOSIS IN TRANSITIONAL CELL CARCINOMA

A survey of the literature reveals surprisingly few studies on the relative malignancy of squamous cell carcinoma and transitional cell carcinoma. According to Quick and Cutler,[5] transitional cell carcinoma is a relatively malignant tumor with a tendency towards distant metastases which may dominate the clinical picture. Ewing[2] likewise considered transitional cell carcinoma as generally more malignant than squamous cell carcinoma of the same region. In view of a dearth of corroborative evidence by other authors, we compared clinically the 27 transitional cell carcinomas in this series with 11 atypical forms and 67 squamous cell carcinomas of the upper respiratory tract. This comparison was made (1) from the standpoint of all the tumors as a whole regardless of location, and (2) according to individual organ sites.

Fig. 3. Carcinoma arising in the mucous membrane of the nose. Similar tumor as seen in Figs. 1 and 2. Note, however, the more apparent carcinomatous nature. (Hematoxylin eosin preparation X150.)

A general survey of squamous cell carcinoma, atypical carcinoma, and transitional cell carcinoma in the upper respiratory tract from the standpoint of regional metastasis, distant metastasis, and longevity under similar treatment (in this group almost all received radiation) revealed the following: (1) All types had a tendency to metastasize to the regional lymph nodes. There was no appreciable difference in this respect between the transitional cell carcinoma (44%) and the squamous cell carcinoma (41%). However, the atypical carcinomas showed this tendency much more than either of the other types (73%). (2) Distant metastases occurred in 13% of the squamous cell carcinomas and in 12% of the transitional cell carcinomas. Evidence of metastasis was obtained by postmortem and X-ray examination. Unfortunately neither of these procedures was employed in the "atypical" carcinomas. Thus the incidence of distant metastases of the transitional and squamous cell carcinomas in our series is about the same. (3) The average longevity with radiation therapy was 23 months in the squamous cell group, 28½ months in the transitional cell group, and 26 months in the atypical group. Fourteen percent of the patients with the squamous cell carcinoma, 24% of those with the transitional cell carcinoma and 36% of those with the atypical carcinoma were still alive after two years. It would seem, therefore, that transitional cell and atypical carcinomas have a better prognosis with radiation therapy than squamous cell carcinoma.

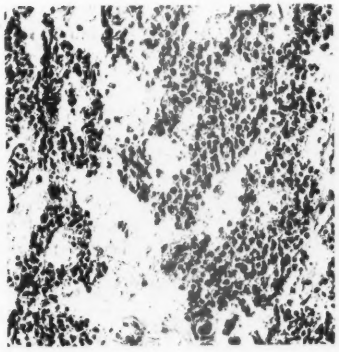

Fig. 4. Transitional cell carcinoma of the antrum (small cell type). The cells are arranged in small masses. The nuclei filling most of the cells are round, oval or spindle shaped and hyperchromatic. (Iron hematoxylin eosin preparation X130.)

TRANSITIONAL CELL CARCINOMA IN VARIOUS ORGANS

Nose.—Transitional cell carcinomas in this region have been variously called cubocellular carcinoma, papillary carcinoma, transitional cell carcinoma and basal cell carcinoma. In our series four such tumors were present. Of these, one metastasized to the cervical lymph nodes. None was known to have metastasized to distant organs. However, only one autopsy was performed. In view of the absence of squamous cell carcinoma in the nose in this series, no comparison can be made between these two types of tumor.

Paranasal sinuses.—Four transitional cell carcinomas were present in this series. Comparison of these with the five squamous cell carcinomas and the one atypical carcinoma (all of which were treated with radiation) revealed the following: (1) Metastasis to the cervical lymph nodes occurred once in both the squamous and transitional cell groups, while none was noted in the one atypical carcinoma. (2) A single autopsy in the squamous cell group disclosed distant metastases (brain), while one autopsy in the transitional cell group revealed no distant metastases. However, skeletal metastases were seen on X-ray examination in two of the patients with transitional cell carcinoma after the tumor had been known to be present for almost four years. No autopsy was performed on the patient with the atypical carcinoma. (3) With radiation therapy the duration

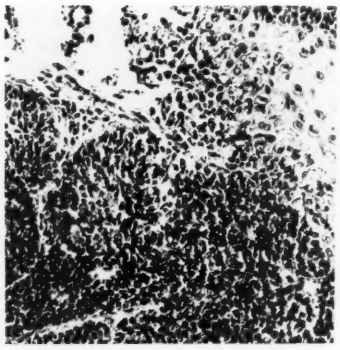

Fig. 5. Transitional cell carcinoma of the pharynx (medium cell type). Note the resemblance to basal cell carcinomas of the skin. However, there is greater variation in size, shape and staining quality. (Iron hematoxylin eosin preparation X130.)

of life in the squamous cell carcinoma was 27 months or less, while three of the four transitional cell carcinomas permitted a survival of four years. The patient with the atypical carcinoma died at the end of 20 months. Thus, although no definite conclusions can be drawn from such a small series, there is an indication that both squamous and transitional cell carcinomas of the paranasal sinuses may metastasize to distant organs but apparently only do so late. Regional metastases may occur, but this is not a prominent feature. With radiation therapy transitional cell carcinoma probably bears a better prognosis than the more radio-resistant squamous cell carcinoma in the paranasal sinuses.

Oral cavity.—Clinical and histologic correlations of carcinoma of the mouth and tongue are meager. Simmons[28] found a rapidly fatal type and a slow growing type of carcinoma of the tongue and mouth, but did not distinguish these two types histologically. Ewing[6] stated that despite considerable variation in clinical malignancy and corresponding structure, most tumors of the tongue were radio-resistant. Phillips[29] found Broders' classification of value in indicating the clinical course of these tumors, but he did not distinguish between transitional and squamous cell carcinomas. Sachs[30] presented 147 carcinomas of the tongue, all of which were squamous cell in type. All metastasized to the regional lymph nodes, and 9.7%

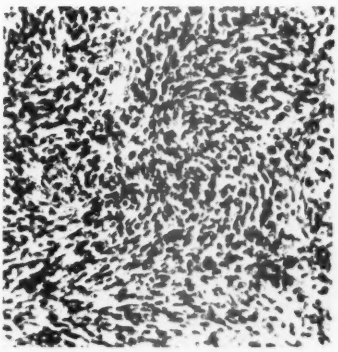

Fig. 6. Transitional cell carcinoma of the antrum (large cell type). Note the spindle shaped tumor cells occasionally showing a plexiform arrangement resembling those seen in certain connective tissue tumors. (Hematoxylin eosin preparation X120.)

showed distant metastases. Gardham[31] pointed out that submucous carcinoma of the posterior third of the tongue was never squamous and responded early to X-ray.

In our series of 15 carcinomas of the oral cavity (excluding tongue), 11 were squamous cell carcinomas, three were transitional cell carcinomas, and one was an atypical carcinoma. All patients had radiation therapy. Clinical comparison of these tumors revealed the following: (1) in the squamous cell group the survival period of 70% of those individuals whose death was directly due to the carcinoma, was between 12 and 24 months. One patient was still alive after three and one-half years without evidence of tumor. Of the three patients having transitional cell carcinomas, one was still alive after three years without tumor. The other two died 18 and 25 months after the appearance of the carcinomas. The patient with the atypical carcinoma was still alive 30 months after the appearance of the tumor. (2) Nine of the 11 squamous cell and one of the three transitional cell carcinomas metastasized to the regional lymph nodes. The atypical carcinoma showed no metastases. (3) Postmortem examinations were too few to allow comparison. It is therefore likely that squamous cell carcinoma and transitional cell carcinoma follow a similar course in the oral cavity.

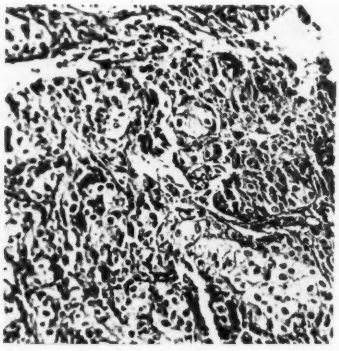

Fig. 7. Carcinoma of the tongue. Note both the squamous and transitional cell characteristics of the individual tumor cell. (Hematoxylin eosin preparation X120.)

There were 15 instances of carcinoma of the tongue in this series, 12 of which were squamous cell, two transitional cell and one an atypical carcinoma. Comparative study revealed the following: (1) metastases to the regional lymph nodes occurred in six of the squamous cell, both transitional cell, and in the atypical carcinoma. (2) Distant metastases occurred in two squamous cell carcinomas; no autopsies were performed in the transitional cell and atypical carcinomas. (3) In the squamous cell group 75% of the patients who succumbed, died from six to 15 months after the appearance of the tumor. Four patients were still alive three and one-half to seven years later without evidence of disease. The patients with transitional cell carcinoma died 16 and 19 months respectively after the onset of the disease. No information as to longevity is available in the patient with the atypical carcinoma. Since there are only two transitional cell carcinomas in this group, valid comparison is difficult. We cannot state whether transitional cell carcinomas have a greater tendency to metastasize than squamous cell carcinomas of the tongue. From the standpoint of longevity there seems to be no difference between these tumors.

Pharynx.—There is a considerable literature on carcinoma of the epi-, oro- and hypopharynx. Yet despite this, one is unable to obtain a clear understanding of the relative malignancy of squamous and transitional cell carcinoma.

In regard to the pharynx in general, Quick and Cutler's[5] conception of transitional cell carcinoma as being a relatively malignant tumor has been previously discussed. Stewart-Harrison[32] classified tumors in this location as epidermoid carcinoma, semi-epidermoid carcinoma and anepidermoid carcinoma. The latter included undifferentiated forms, transitional cell carcinoma and lymphoepithelioma. He mentioned that metastases from the pharynx are common but failed to differentiate the relative malignancy of the various types. New and Figi[33] in their discussion of tumors of the pharynx and tonsil presented 34 cases of squamous cell carcinoma, 11 cases of lymphosarcoma, and 31 cases of adenocarcinoma. They did not mention transitional cell carcinoma. Salinger and Pearlman[34] made a comprehensive study of the terminology employed for tumors in this region, and decided that many so-called lymphosarcomas were probably transitional cell carcinomas. They reported 24 instances of transitional cell carcinoma in which cervical adenopathy was present in 80%.

In the epipharynx, according to Ewing,[6, 7] all tumors with the exception of squamous cell carcinoma are radio-sensitive. The distribution of tumors in his series was: squamous cell carcinomas, 30%; transitional cell carcinomas, 37%; lymphosarcomas, 15%; lymphoepithelioma, 11%; adenoma malignum, 3%; and the epithelioma adenoides cysticum, 4%. Zuppinger and Stewart-Harrison[35] agreed that the vast majority of tumors in this region was highly radio-sensitive, and that all produced extensive metastases. Martin[36] stated that all malignant tumors in this region were radio-sensitive, and that from this standpoint, the histopathologic classification was unimportant. He was impressed by the frequent mediastinal and pulmonary metastases. Martin and Blady[37] found nasopharyngeal carcinomas to represent 2% of all carcinomas. Of 87 nasopharyngeal carcinomas in their series, 42 were transitional cell, 14 lymphoepithelioma, eight squamous cell and four spindle cell carcinomas. The remainder were rare forms. Metastases were the first indication of the tumor in 50% of the patients. Eighty-one percent showed metastases to cervical nodes. General metastases were found in the skeletal system, lungs and liver. The average survival was 14 months. No prognostic distinction was made between transitional and squamous cell carcinoma.

Zuppinger[38] and Ducuing and Ducuing[39] felt that tumors of the walls of the oropharynx should be differentiated from those of the tonsils and other parts of the pharynx because in this region the lymphatic network terminates directly in the retropharyngeal and

upper jugular nodes. Therefore, early metastasis to the lymph nodes is common. Zuppinger presented 15 such tumors and Ducuing and Ducuing eight. Despite the presence of transitional cell carcinomas among these tumors, Ducuing and Ducuing made no distinction as to differences in malignancy of the two histologic types. These authors[40] likewise considered carcinoma of the glossotonsillar recess to be a separate entity. These tumors developed rapidly and, apparently because of the abundant lymphatics, metastasized rapidly to the regional nodes. However, there was no tendency to spread beyond these nodes, and death resulted from local complications. Of the tumors presented, four were squamous cell, four basal cell, and two were atypical. Again no comparison was made as to the relative malignancy of the morphologic groups.

As far as tumors of the tonsil and base of the tongue are concerned, Ewing[7] presented the following histologic types: squamous cell carcinoma, 72%; transitional cell carcinoma, 12%; lymphosarcoma, 9%; lymphoepithelioma, 4%, and other forms, 3%.

Tumors of the hypopharynx include those arising from the postero-inferior portion of the tongue, the valleculae, the pharyngeal aspect of the epiglottis, the lateral and posterior pharyngeal wall, the aryepiglottic folds, and the pyriform sinuses. Those of the pyriform sinuses, epiglottis and aryepiglottic folds will be considered with the carcinomas of the larynx. According to Beck and Guttman,[41] tumors of the lateral and posterior pharyngeal walls are usually fully differentiated squamous cell carcinomas with slow growth and progression, but with metastases to the regional lymph nodes. Tumors of the valleculae and of the aryepiglottic folds, according to Zuppinger and Stewart-Harrison,[35] are less differentiated carcinomas and are highly radio-sensitive.

It is thus apparent from this brief summary that the difference in behavior between squamous and transitional cell carcinoma of the pharynx is not brought out in the literature. Unfortunately, our small series can give only indications as to the relative natures of these tumors.

Comparison of the five squamous cell with the four transitional cell and the three atypical carcinomas of the pharynx (excluding the tonsils) revealed the following: (1) Metastases to the cervical lymph nodes occurred in two of the five squamous cell, three of the four transitional cell, and all of the three atypical carcinomas. (2) As far as survival after radiation is concerned, all of the patients with squamous cell carcinoma lived less than 30 months, while two

of the four patients with transitional cell carcinoma were still alive more than three and one-half years after the onset of symptoms. Among the atypical tumors, one patient was still alive after five years, while the other two died less than two years after the appearance of the tumor. (3) No autopsies were performed in this group. This small series of tumors would suggest that transitional cell and atypical carcinomas have a greater tendency to metastasize to the regional lymph nodes than do squamous cell carcinomas. On the other hand, with radiation therapy transitional cell carcinomas and possibly atypical carcinomas bear a better prognosis than squamous cell carcinomas. The question of distant metastasis is not answered in the study of these patients.

Comparison of the four squamous cell with the two transitional cell and the one atypical carcinoma of the tonsil revealed the following: (1) Metastasis to the regional lymph nodes occurred in three of the four squamous, one of the two transitional cell, and in the one atypical carcinoma. (2) Of the four squamous cell carcinoma patients, three succumbed five, 10 and 12½ months respectively after the onset of symptoms, while a fourth was still alive after two years without tumor. Of the two patients with transitional cell carcinoma, one died one year after onset of symptoms, and the other was still alive after four and one-half years without evidence of disease. The patient with the atypical tumor was still alive without symptoms four years after the appearance of the tumor. There is thus an indication that all types of carcinoma of the tonsil tend to metastasize to the regional lymph nodes, but that with radiation therapy the prognosis is better in transitional cell and atypical tumors.

Larynx.—Here as elsewhere the literature is replete with differences in nomenclature, although there is greater unanimity of opinion as to prognosis of tumors in various parts of the larynx. Yet, as elsewhere, the difference in behavior, if any, between squamous and transitional cell carcinomas is not clear.

Tumors may be classified as extrinsic or intrinsic. Extrinsic tumors include those of the pyriform sinuses, aryepiglottic folds and pharyngeal aspect of the arytenoids and epiglottis. Intrinsic carcinomas include those of the laryngeal aspect of the epiglottis, the vocal cords, the subglottic region, the false cords and the ventricular cavity. In the literature on intrinsic carcinoma, Coutard and Valat[12] stated that carcinoma of the epiglottis spread rapidly and early to the regional lymph nodes. In their series, carcinoma of the vocal

cords was usually of the cutaneous squamous cell type with good prognosis, although radio-resistant. Carcinoma of the subglottic region was usually a squamous cell carcinoma of the mucous membrane type with less marked differentiation and incomplete stratification. It was very radio-sensitive, and tended to metastasize to the lymph nodes. Zuppinger and Stewart-Harrison[35] found tumors of the false cords to be highly radio-sensitive. Beck and Guttman,[43] among 72 carcinomas of the larynx, found three transitional cell carcinomas. They were impressed, as were Quick and Cutler,[5] in respect to all transitional cell carcinomas of the upper respiratory tract, with the greater malignancy of the latter in comparison to the squamous cell variety. Tucker[44] found among 200 malignant tumors of the larynx, 191 squamous cell carcinomas, eight basal cell carcinomas, and one sarcoma. Leroux-Robert[45] stressed that vocal cord carcinoma tends to remain localized, while vestibular, ventricular, and subglottic epitheliomas tend to infiltrate. He classified carcinomas into basocellular or undifferentiated carcinoma, intermediary, and true epithelioma of the skin and mucous membrane type. The most common type of carcinoma of the vocal cords in their series was the epithelioma of the mucous membrane type; less common was the cutaneous type. On the false cords and in the ventricle the tumors were so-called basocellular carcinomas, epitheliomas of the mucous membrane type, and incompletely differentiated epitheliomas with predominance of basal cells. In the subglottic region, the cutaneous and mucous membrane type and undifferentiated carcinoma were of equal frequency. He did not compare the relative malignancy of the various histologic forms.

Various authors have tried to correlate the histologic features of tumors of the larynx with their malignancy. Graham,[46] Grahe,[47] Soerensen,[48] and Portmann and Despons[49] found that the histologic structure of tumors of the larynx gave no indication as to their degree of malignancy. Clerf and Crawford[50] differentiated tumors of the larynx according to Broders' classification. Some fell into Groups 1 and 4, but most fell into the intermediary groups. There was a large number of recurrences in the intermediary groups as well as in Group 4. They, therefore, questioned the value of this grading. However, in several anaplastic tumors metastasis occurred early. Hlávacek[51] found that a larger number of mitoses did not indicate a greater malignancy of a tumor. However, the degree of differentiation was a good guide. More important in this respect was the location of the tumor. Intrinsic carcinomas which were limited to the vocal cords or extended as far as the recess of Morgagni gave a

better prognosis than intrinsic tumors present in the subglottic space. Whenever lymph nodes were involved, the tumor had extended to or was present in the epiglottis, subglottic space, and the cricoid region. Those that had metastasized were both spinous and basocellular. He did not discuss the difference in maligancy between these two types. Harris and Klemperer[52] found little difference in the degree of differentiation or atypism between radio-sensitive and radio-resistant tumors of the larynx. The only difference was in the number of mitoses.

In regard to extrinsic tumors of the larynx, Von Eicken[53] stated that tumors of the pyriform sinus grow rapidly and metastasize early. Beck and Guttman[41] found that these tumors were most often transitional cell carcinomas or lymphoepitheliomas. Ducuing and Ducuing,[54] however, found that 60% of these tumors were spinous cell carcinomas, 20% atypical carcinomas, 18% basal cell carcinomas, and 2% other types. The most prominent first symptom was lymphadenopathy. In Zuppinger's[55] series, 50% were squamous cell carcinoma with keratinization, 10% without keratinization, 36% epithelioma solidum simplex, and 4% other forms.

Beck and Guttman[41] indicated that tumors of the aryepiglottic fold were most often squamous cell carcinomas, less often transitional cell carcinomas or lymphoepitheliomas. Metastases to the lymph nodes were constantly found. Zuppinger and Stewart-Harrison[35] found these tumors to be very radio-sensitive. Zuppinger[56] described tumors of the retrocricoid region, of which 15 were squamous cell carcinomas with cornification, one, a squamous carcinoma without cornification, two carcinomas simplex, and one uncertain. Ducuing and Ducuing[57] described seven such tumors, two atypical epitheliomas, two basocellular carcinomas, two spinocellular carcinomas with cornification, and one indefinite. Metastases to the lymph nodes were frequent in these patients, but no visceral or osseous metastases were noted.

It is thus apparent that the whole question of the relative malignancy of the squamous or transitional cell carcinomas in the larynx is not thoroughly discussed in the literature. Only Quick and Cutler,[5] Ewing,[8] and Beck and Guttman[43] have dealt with the subject, and their opinions were that transitional cell carcinomas are more malignant than squamous cell carcinomas.

In our series 42 instances of carcinomas of the larynx were studied. These were classified according to location as follows: Fourteen were limited to the true and false cords and the ventricle;

ten arose from the cords and the interior of the larynx but had spread to extrinsic structures; six were primary tumors arising in the region of the arytenoids; two were subglottic tumors; five were tumors of the epiglottis; and five involved the pyriform sinuses.

Comparative study of the three transitional cell and the 11 squamous cell carcinomas which were limited to the cords and ventricle reveal the following: (1) None of the tumors of either type metastasized to the regional lymph nodes; (2) no autopsies were done in this group; (3) no comparative study of survival could be made because of variations in treatment. This small series would tend to indicate that neither squamous cell nor transitional cell carcinomas which remain localized to the vocal cords tend to metastasize. Comparative study of the nine squamous cell carcinomas and the one transitional cell carcinoma arising intrinsically but which extended to extrinsic structures revealed the following: (1) Three of the squamous cell which had invaded the arytenoids and the one transitional cell carcinoma which had reached the cricoid, metastasized to the regional lymph nodes; (2) postmortem examination on two patients with squamous cell carcinomas revealed no metastasis. No autopsy was done on the patient with the transitional cell carcinoma. These facts would seem to indicate that both transitional cell and squamous cell carcinomas which extend to extrinsic structures may metastasize to the regional lymph nodes. Because of the small series, we cannot conclude whether or not intrinsic transitional cell carcinomas have a greater tendency than squamous cell carcinomas to spread extrinsically.

Altogether there were 13 tumors (ten squamous, one transitional and two atypical carcinomas) which involved the arytenoids either primarily (six tumors) or secondarily (seven tumors). Four of the squamous cell, the one transitional cell and the two atypical carcinomas metastasized to the regional nodes. Of the six primary arytenoid carcinomas, one of the three squamous, the one transitional and the two atypical carcinomas showed regional lymphadenopathy. Two autopsies performed on patients with squamous cell carcinoma revealed no distant metastases. X-ray examination of the patient with transitional cell carcinoma, however, revealed pulmonary metastases. This material indicates that when the arytenoids are involved, there is a tendency towards regional metastasis.

Comparative study of the two squamous and the three transitional cell carcinomas of the epiglottis revealed the following: (1) Metastases to the regional lymph nodes occurred in one squa-

mous cell carcinoma and in one transitional cell carcinoma; (2) no postmortem material was available for study, but X-ray of the chest revealed pulmonary metastases in one transitional cell carcinoma. From this small series there is thus an indication that both squamous and transitional cell carcinomas of the epiglottis metastasize to the regional nodes. The relative tendency of each to metastasize cannot be estimated from this small series.

Four squamous cell and one atypical carcinoma of the pyriform sinus were present in this series but no transitional cell carcinoma. Two of the squamous and the atypical carcinoma showed local metastasis. Three patients with squamous cell carcinomas came to autopsy, of whom one showed distant metastases (lung). This indicates that the squamous cell carcinoma of the pyriform sinus tends to metastasize to the regional nodes and possibly further. We have no material on the relative malignancy of squamous and transitional cell carcinoma of the pyriform sinus.

Of the two subglottic tumors in this series, one was an atypical carcinoma with no local metastasis. The other, a squamous cell carcinoma, gave rise to regional metastasis.

In summary, 42 laryngeal carcinomas were studied, 30 of which were squamous cell, eight transitional cell and four atypical carcinomas. Twenty-seven percent of the squamous, 38% of the transitional cell, and 75% of the atypical carcinomas metastasized locally. Distant metastasis was known to have occurred in three patients, one with squamous cell carcinoma and two with transitional cell carcinomas. Three postmortem examinations on patients with squamous cell carcinomas failed to reveal any evidence of distant metastasis.

From this small series there are indications that: (1) intrinsic tumors of the larynx do not metastasize, regardless of morphology; (2) tumors which involve the arytenoids, the cricoid, the epiglottis and the pyriform sinuses may metastasize. Transitional cell and atypical carcinomas tend to metastasize somewhat more readily than squamous cell carcinomas in extrinsic locations.

COMPARATIVE CLINICAL STUDY OF TYPES OF TRANSITIONAL CELL CARCINOMAS

A further clinical study was made of the morphologic types of transitional cell carcinoma—the small, medium and large basal cell types, and the nasal. Metastasis to the regional lymph nodes occurred in 100% of the small, 44% of the medium sized, 41% of the large,

and 25% of the nasal. The small number of cases in the small and nasal groups do not permit drawing any conclusions; and there is very little difference between the medium and large cell groups from the standpoint of local metastasis. From the standpoint of survival, there was no difference between the various types with the exception of the medium basal cell type. Patients in this group survived as long as 39 months in comparison to the usual survival of two years for the other groups. Perhaps correlated with this is the greater incidence of distant metastasis in this group.

Comparison was also made between the clinical malignancy of the tumor and the number of mitoses on the one hand, and the difference in size, shape and staining quality of the cells on the other. This showed that: (1) from the standpoint of survival with radiation therapy, there was no difference between those with few and those with many mitoses; (2) from the standpoint of metastasis to the regional lymph nodes the tumors with more mitoses metastasized to a certain extent more readily. From the standpoint of atypism, local metastasis was more frequent in the carcinomas with moderate cell variation than in the group with marked cell variation. From the standpoint of survival there was no difference between tumors with varying degrees of cellular atypism. This would seem to indicate that the difference in size and shape and staining quality is a less important criterion for the degree of malignancy than the number of mitoses. This is understandable in view of the effect of tissue environment on tumor cells.

SUMMARY AND CONCLUSIONS

A review of the literature on transitional cell carcinoma of the upper respiratory tract reveals controversy as to the morphological appearance, nomenclature and prognosis of these tumors. Confusion is also encountered in regard to so-called lymphoepithelioma. The histologic characteristic features of transitional cell carcinoma are: cylindrical, fusiform, or oval tumor cells; a tendency towards a whorled arrangement of the tumor cells; hyperchromatic nuclei, and scant cytoplasm with a tendency towards basophilia. The most striking difference between the various tumors was the variety of sizes of the tumor cells.

The relative merits of various terminology of these tumors are discussed. Despite valid objections, the term transitional cell carcinoma is retained. Upon the basis of morphologic studies, malignant tumors of epithelial origin are classified as: squamous cell car-

cinoma; transitional cell carcinoma; squamous cell carcinoma with transitional cell features, and vice versa; and atypical carcinoma. Adenocarcinoma did not fall within the scope of this study.

Squamous cell carcinoma probably arises from those cells of the basal layer which have a tendency to go on to cornification. Transitional cell carcinoma occurring in stratified squamous epithelium probably arises from those cells of the basal layer which retain their basal cell characteristics and do not go on to cornification. When the tumor occurs in the region of pseudostratified ciliated columnar epithelium, it may arise from any of the cells.

A general comparative clinical study of the relative malignancy of squamous cell, transitional cell and atypical carcinoma of the upper respiratory tract regardless of specific location reveals that there was no special difference between transitional cell and squamous cell carcinoma insofar as regional and distant metastases are concerned. Atypical carcinoma, however, showed a greater tendency towards regional metastasis than the other two types. With radiation therapy the prognosis was better for the patients with transitional cell and atypical carcinoma than for those with squamous cell carcinoma. A comparative clinical study of the three types of tumors according to location shows that with radiation therapy transitional cell carcinoma of the pharynx, antrum and tonsil had a better prognosis than squamous cell carcinoma in the same region. Tumors restricted to the vocal cords did not metastasize regardless of whether they were transitional or squamous cell carcinomas. Extrinsic tumors of the larynx, both transitional cell and squamous cell, metastasized to the regional lymph nodes.

The number of mitotic figures in the transitional cell carcinomas seems to be a more important criterion for the evaluation of the degree of malignancy than cellular atypism.

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XXVIII

UNUSUAL TUMORS OF THE UPPER RESPIRATORY TRACT*

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The purpose of this paper is to record and to discuss the pathology of a series of unusual tumors encountered in the upper respiratory tract. It is not statistical nor does it deal with diagnosis and treatment.

RHABDOMYOSARCOMA OF THE POSTERIOR SEPTUM

A boy six years of age, after measles, developed nasal obstruction, although he had had his tonsils and adenoids removed one year previously. Examination showed a new growth filling the postnasal space and apparently originating from the posterior border of the septum. Removal of the tumor and microscopic sections revealed it to be a rhabdomyosarcoma. The maximum dosage of external radiation was used, but the tumor recurred and had again to be removed. At this time the patient came under my (L.A.S.) care.

Both posterior choanae were filled with tumor, which arose from the posterior border and margins of the nasal septum. The tumor was approached by the removal of the entire nasal septum, the surgery being supplementing by the local application of 600 mg. hours of radium radiation. During the next ten months this patient underwent two lateral rhinotomies for recurrences as well as receiving the maximum dosage of radiation both locally and externally. The terminal stage was characterized by cervical, pharyngeal and mediastinal metastasis.

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*Read before the American Laryngological Association, May 27, 1940, Rye, New York.

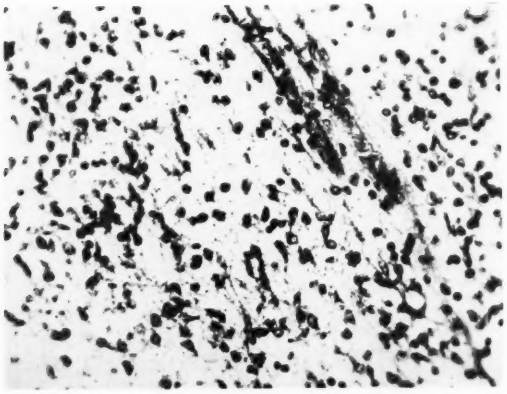

Fig. 1. Rhabdomyosarcoma of posterior septum.

Tumors consisting of striated muscle are not only very rare, but according to Boyd[1] they do not occur in voluntary muscle. They are usually found in the kidney, testicle, vagina. A pure rhabdomyosarcoma is the rarest of all being practically confined to the heart. They are common in children, and probably arise in embryonic rudiments. In this neoplasm, the muscle is mingled with other tissues, and only some of the cells are cross-striated. These mixed tumors are highly malignant, and metastasize by the blood stream. The structure of rhabdomyosarcoma presents chiefly a system of parallel bundles of intertwining strands of striped muscle fibers, supported by adult or embryonal connective tissue. The cells of this tumor seldom exhibit characteristics of mature cells. They are usually thin and much elongated and rarely branching. Both longitudinal and cross striations may be pronounced; the cross striations may be present in a part of the cell only, or be entirely missing. In large vacuolated cells Ribbert[2] describes concentric striations of the perinuclear cytoplasm. In the more embryonal types, the cells are spindle shaped, shorter, and even round, and may lose their acidophilic character and all resemblance to muscle cells. Yet such marked anaplasia is seldom, if ever, universal. Certain foci commonly retain cells of myogenic character.

The nuclei follow a type with a large vesicular chromatic body, single or multiple, which lies in a central area of granular cytoplasm. The stroma may be loose, adult, connective, embryonal, sarcomatous,

or myxosarcomatous in type, and cartilage and various other kinds of tissue may be present. Blood vessels are usually abundant and occasionally are markedly overdeveloped.

In this particular tumor the outstanding feature is the great number of mitotic figures. Here and there parallel bundles of muscle fibers may be seen supported by a slightly staining connective tissue. This tumor is not radio-sensitive, and the treatment should be surgical.

OSTEOGENIC SARCOMA OF THE MAXILLARY ANTRUM

A white male, 24 years of age, complained of pain in the left upper teeth. After repeated dental consultations, one of the dentists took X-rays of the sinuses, which were interpreted as showing a left chronic maxillary sinusitis. A Caldwell-Luc operation was attempted in the office, and the patient was referred when the removal of the tissue from the antrum was followed by profuse hemorrhage.

Operative treatment consisted of a modified Moure operation, with the local use of radium. Eighteen months afterwards, the tumor recurred, and in the next eighteen months he underwent thirteen operations including an exenteration of the orbit for removal of the recurrence, as well as the maximum use of both radium and external radiation.

According to Boyd,[2] this neoplasm is "the most important, the most malignant, the most common, and the most perplexing of all the tumors of bone." Spread of the tumor takes place by the blood stream, although in exceptional cases lymph nodes may be involved. Metastasis occurs most often in the lungs, and these should be X-rayed before surgical removal of the tumor is considered. To find this sarcoma in any position in the body except the long bones is indeed rare.

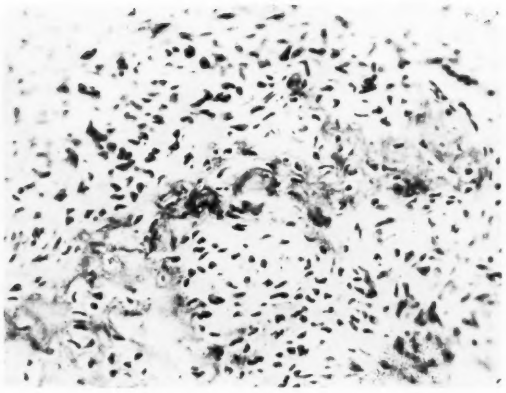

Fig. 2. Osteosarcoma of maxillary sinus.

The microscopic appearance is probably more varied than that of any other neoplasm. The tumor cells are osteoblasts, but these vary greatly in the degree of differentiation which they attain and the type of intracellular material which they produce. The predominant cell type is a small spindle cell with hyperchromatic nucleus and poorly defined cell borders. Cellular pleomorphism is one of the chief characteristics of osteogenic sarcoma, and its degree is probably the best indication of the malignancy of the tumor. The characteristic feature of an osteogenic sarcoma is not its cells but the intercellular substance which these cells produce. This may take any of five forms, hyaline and fibrous, cartilaginous, myxomatous, osteoid, and osseous.

This section shows the typical spindle cells and very little cellular pleomorphism. Numerous areas of new bone are present, one of which is shown in the center of the photomicrograph. Obviously, this sarcoma is of the osseous type, not highly malignant, and probably not prone to metastasize readily because of the evident lack of vascularity. Osteogenic sarcoma when involving the facial bones is much less maligant than when it occurs in the long bones.

NEUROFIBROMA OF THE VOCAL CORD

A public speaker, 54 years of age, was hoarse for over a year. Laryngeal examination showed a pea-sized, smooth, pedunculated growth springing from the upper surface of the anterior third of the right vocal cord. Removal and microscopic examination revealed it to be a neurofibroma. There was no previous, nor has there been in the year since removal, any evidence of other neurofibromas.

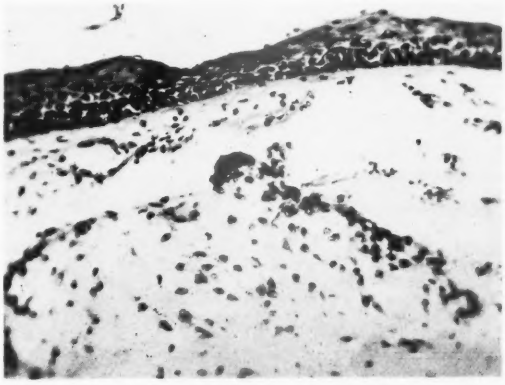

Fig. 3. Neurofibroma of vocal cord.

Any discussion regarding tumors of nerves immediately plunges one into a very confusing and complex subject. Each pathologist has, from time to time, differentiated and classified these tumors until one finds a number of them which have histologically much in common, masquerading under very different names. Among these may be mentioned the following: acoustic nerve tumor, perineural fibroma, neuro-fibroma (von Recklinghausen's disease), neurogenic fibroma and sarcoma. All of these arise from the specialized investments which separate and insulate nerve tissue from surrounding structures. They are usually regarded as fibroblastomas, innocent or malignant, arising from the connective tissue sheath (perineurium) of nerves so that they have been called perineurial fibroblastomas. The French school, conversely, of whom Masson[4] is the chief expo-

nent, contends that they arise from the cells of the sheath of Schwann (Schwannomas), and are, therefore, ectodermal in origin. However, leaving the classification to the professional pathologist, an examination of the different tumors will show the following features in common: long, slender, wire-like fibers, with elongated nuclei which have a tendency to be arranged in parallel or palisade fashion. In addition to this palisading which always suggests a nerve sheath origin, the nuclei may be grouped in eddies and streams. The more benign the tumor, the more pronounced are these features. In numerous cases, the subcutaneous and deeper nerve trunks and especially the peripheral portions of the nerve trunks, are the site of single or multiple tumors, which are usually more cellular than the cutaneous fibromas and, according to Ewing, carry a much more serious prognosis.

In the simplest form the tumor is a firm, movable mass, lying in the subcutaneous tissues, well circumscribed, of moderate dimensions, of slow growth, and often permitting successful exicision, such as in this particular case.

It is easily seen how this tumor is covered by an extremely thin squamous epithelium. Because of the lack of characteristic palisading and definite morphological groupings of the cellular elements, it is to be assumed that this neoplasm is probably malignant in nature.

HYPERNEPHROMA OF THE MAXILLARY ANTRUM

A white male, aged 50, had the left kidney removed in 1933 due to a new growth. Four years later, he developed an acute upper respiratory infection with bloody nasal discharge. The patient was seen through the courtesy of Dr. Harold G. Tobey. Examination and operation showed a hypernephroma of the left maxillary antrum. He has remained free from recurrence since the operation in 1937.

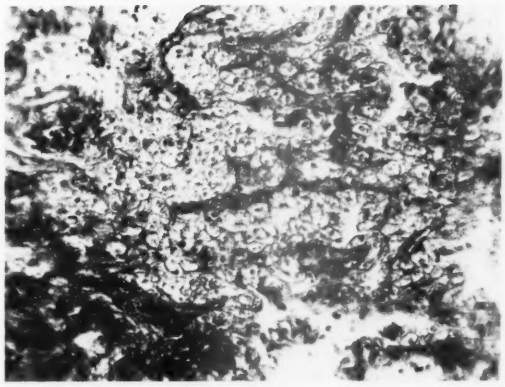

Fig. 4. Hypernephroma of maxillary antrum.

The primary site of this tumor is usually the upper or lower pole of the kidney where it appears as a rounded mass, at first encapsulated and later, according to Boyd,[6] invasive. When one sections this tumor the variegated appearance of the cut surface is striking. It is always yellow in color, due to lipoid material, admixed with red hemorrhagic areas and cysts of varying sizes.

Microscopically, the picture is quite characteristic. The cells are rounded and large, with a peculiarly clear and vacuolated cytoplasm. The clearness and vacuolization is due to the presence of a large amount of lipoid, dissolved from the section in the staining process. This lipoid is mostly cholesterol ester. The stroma is scanty but blood vessels form a striking feature of the picture. They are usually numerous and very large, and the vessel walls often seem to be formed of tumor cells. This arrangement accounts for the frequent hemorrhages into the tumor and the tendency to metastasize by the blood stream. Metastasis most frequently takes place to the lungs and heart, but the regional lymph nodes are involved via the lymphatics.

Hypernephroma is one of the most important causes of secondary tumors of bone. Frequently the first indication that there is any pathology present may be the occurrence of a spontaneous fracture.

An examination of this section makes it immediately evident that the tumor cells seen are those of a typical hypernephroma, being

large and rounded with a peculiarly clear and vacuolated cytoplasm. The stroma is thin suggesting poor support, and blood vessels are seen throughout. Of all the tumors which may be found in the region of the nasopharynx and sinuses probably the most amazing is a hypernephroma. Obviously this is a metastatic tumor.

PLASMOCYTOMA OF THE NASOPHARYNX

A white male of 68 years complained of right-sided nasal obstruction for six months but did not seek medical advice until he had nasal bleeding. Examination revealed a large (egg sized) new growth of the right nasopharynx. The growth was smooth, bluish in color, and attached to the right pharyngeal wall, extending to the orifice of the eustachian tube.

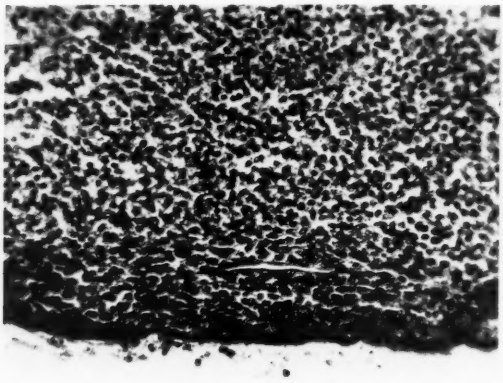

Fig. 5. Plasmocytoma of nasopharynx.

Plasmocytomas in the field of otolaryngology are infrequently encountered; the literature does not contain many reports of this neoplasm found in the nasal mucosa of the nasopharynx. When one considers the comparative frequency of plasma cell tumors of the mucous membrane and lymph nodes, inadequate attention has been given this subject. In a review of the literature Claiborn and Ferris[7] in 1931 found only 12 cases, to which they added two of their own. The number of cases from the Massachusetts Eye and Ear Infirmary in recent years has totaled six.

The distinctive characteristic of this tumor is found in the cellular elements, and the neoplasm is, as the name implies, entirely composed of plasma cells. The origin of these cells is still a debatable point. Mallory[8] believes that some of the lymphocytes undergo a change in the tissues and appear in a form to which the term "plasma cell" is applied. The cell is usually somewhat larger than a lymphocyte, with cytoplasm which is basophilic. The nucleus, which is usually single but which may occasionally be multiple, is small and eccentrically placed.

This section shows the orthodox arrangement of the cells, massed together with little supporting stroma. Here and there throughout the section one may see the more darkly staining lymphocytes, this being due to the fact that the normal lymphoid tissue of the nasopharynx has been invaded, hence the presence of both types of cells. Numerous mitotic figures are present.

The most frequently encountered plasmocytoma is that of multiple myeloma of bone, and its relationship to the plasmocytomas found in otolaryngology must be considered. In this respect the roentgenologic picture must be part of the diagnostic armamentarium. Jackson, Parker and Bethea[8] reported a case which extended over a period of eight years before skeletal involvement was noted.

EWING'S TUMOR OF THE SPHENOID

A physician, 25 years of age, in September 1938 developed a pain in the left hip, which radiated down the thigh. He paid but little attention to it for several days but finally submitted to an X-ray examination which showed an area of destruction of the ilium and the rim of the acetabulum. A biopsy from the ilium revealed the disease to be a so-called Ewing's tumor. Massive dosage of external irradiation was given both locally and then generally for metastasis that developed in the ribs, sternum and humerus. The terminal stage was complicated by the neurological symptoms of headache, diplopia (sixth nerve paralysis), strabismus and anesthesia of the left lower jaw.

At autopsy in September 1939 there was not only general metastasis but involvement of the left sphenoid and ethmoid.

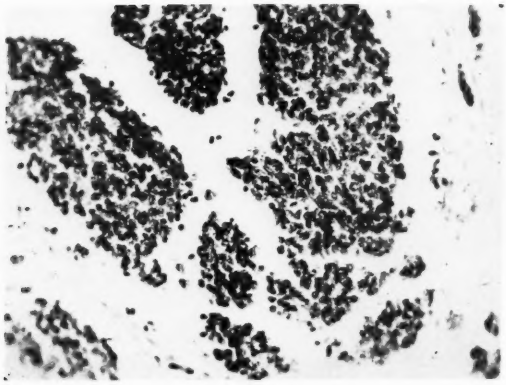

Fig. 6. Ewing's tumor of sphenoid.

In 1920 Ewing[9] began to separate from the general mass of malignant bone tumors one which he considered an endothelioma. There appears to be no doubt that it forms a very definite entity and one which has aroused among pathologists a remarkable amount of interest in the last few years. Over 80% of the cases occur before the age of 30, the majority occurring between 5 and 11 years of age. This disease process frequently commences in one of the long bones. The tumor is usually very soft and may resemble brain tissue. It first destroys the bone and then invades the surrounding soft parts. Some cases have been regarded as osteomyelitic until the true nature of the tumor was discovered by pathologic section.

The microscopic picture is quite definite. There is a uniform arrangement of round or polyhedral cells which in the past has given rise to a diagnosis of round cell sarcoma of bone. The nucleus is small and round and the cytoplasm is clear. The cell forms no intracellular substance, in striking contrast to the cells of osteogenic sarcoma. These cells may be arranged as a lining for blood spaces and sinuses, the angio-endotheliomatous form, or they may be arranged in sheets, the diffuse form. One of the most important features of the tumor is its tendency to metastasize to other bones, the skull, the sternum, vertebrae and ilium being the areas of predilection. Secondary growths in the lungs are commonly found at autopsy. This tumor is remarkably sensitive to radiation as opposed to an osteogenic sarcoma, which is rather resistant; hence this reaction is of great diagnostic value.

It is apparent from this section that this tumor falls into the group with diffusely arranged cells. Masses of closely packed, round and polyhedral cells may be seen. The stroma is lightly staining, loose connective tissue containing several good-sized blood vessels. It is interesting to note the similarity of these cells to those of the plasmocytoma.

OSTEITIS FIBROSA OF THE MAXILLARY ANTRUM

A girl 19 years of age sought medical advice because the right side of the face for the past eight years was growing progressively larger than the left. Other than the disfigurement there had been no discomfort.

Examination showed a marked asymmetry of the face due to a hard smooth swelling of the right superior maxilla extending up to the infraorbital rim.

At operation the right maxillary antrum was found filled with firm fibrous-like tissue.

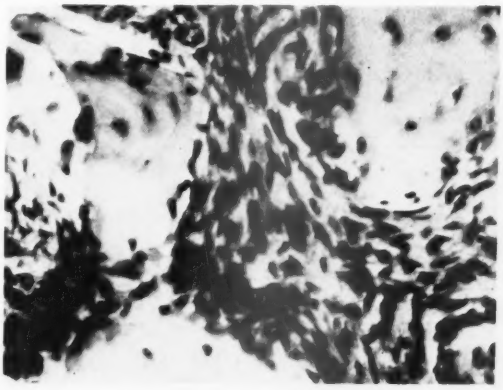

Fig. 7. Osteitis fibrosa of maxillary antrum.

This disease must be differentiated from osteitis fibrosa cystica, in which cyst formation may be a striking feature of the pathological picture; but such formation is secondary and not essential to the condition. There are two forms of osteitis fibrosa cystica, the first localized and common, the second generalized and rare. The generalized form was first described by von Recklinghausen in 1891, and it is now known that in the majority if not in all cases, the disease is a manifestation of hyperparathyroidism. Boyd[11, 12] states that the

blood calcium rises from the normal of 10 mg. per 100 cc. to 14 or 15 mg. while the blood phosphorus remains low, but the plasma phosphatase is considerably raised.

This particular tumor represents a non-cystic form in which sclerosis is predominant. The blood findings are normal. This form bears no relation to the generalized disease, and is not dependent on hyperparathyroidism for its etiology. It usually appears in adolescence, and after progressing for a number of years, it may undergo spontaneous recovery. Solitary bone cysts may appear in the long bones. Small giant cell tumors may develop in the wall of the cyst, and the pathological features are therefore quite similar to those of generalized osteitis fibrosa. The exact nature of the condition is obscure, but it may be a perversion of the normal process of removal of calcified cartilage by vascular connective tissue preparatory to the formation of true bone.

In this section the bony trabeculae are slightly increased in thickness with a predominance of osteoblasts. There is a diffuse replacement of the marrow with well-differentiated connective tissue cells containing a moderate amount of collagen.

MENINGIOMA OF THE PHARYNX

Through the courtesy of Dr. Samuel Cline, we are able to report the patient L. B., aged 24, female, who noticed a swelling in the right side of her throat which had been growing larger over a period of four months. Examination showed a mass the size of a walnut just behind the right posterior pillar. This mass could also be palpated from the outside under the angle of the jaw.

At operation to obtain a biopsy a firm irregular mass was found extending from beneath the posterior border of the submaxillary gland in intimate contact with the common facial vein, the hypoglossal nerve, and the external carotid artery. The mass extended proximally beneath the ramus of the mandible, and posteriorly toward the base of the skull and upper cervical vertebrae. In order to remove this portion of the mass it was necessary to ligate the facial vein, to cut the right hypoglossal nerve, and to peel the mass off the external carotid artery.

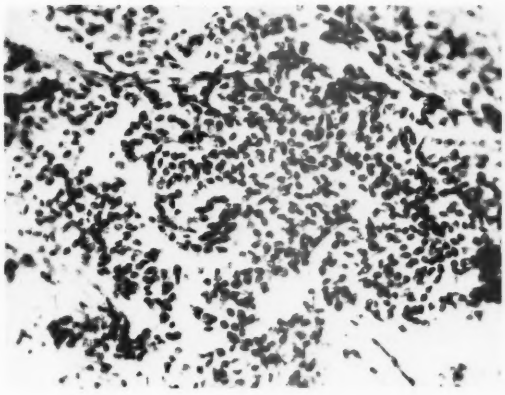

Fig. 8. Meningioma of pharynx.

A large number of names have been applied at various times to this tumor, the most common name being dural endothelioma. Harvey Cushing[11] has suggested the term meningioma, which in many ways is preferable to any of those in use. This neoplasm is not a true tumor of the brain because it does not arise from the brain substance. Its common name suggests that it arises from the dura mater, but this, too, is a misnomer, for its site of origin is the arachnoid, in those groups of mesothelial cells which are found in connection with, or close to, the arachnoid villi. Meningiomas are also found in the spinal canal where they take origin from the arachnoid at the point of emergence of one of the nerve roots. Rarely they are found at the foramina of exit of the cranial nerves, particularly the second, fifth and eighth.

Microscopically, the tumor consists of masses of elongated cells which may show a whorled arrangement. It is usually well encapsulated and readily shells from its bed.

This particular section shows the classical whorled arrangement of the cells, and the tumor was easily removed. Because of its location, it is assumed that it emerged from the foramen of the fifth nerve.

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XXIX

FRONTAL SINUSITIS*

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CLINICAL ANATOMY

Infantile Development of Frontal Sinus.—The frontal bone is of membranous origin, consisting at birth of two halves which begin to unite at one year, and usually undergo fusion along the metopic suture during the second year. Occasionally this union is delayed and sometimes never occurs.

During the fourth or fifth month of fetal life the frontal sinus begins to develop from an anlage in the frontal recess of the middle meatus. It may also start from an anterior ethmoidal cell or even by extension from the infundibulum ethmoidale. A double or triple frontal sinus on one side is proof of the variation possible in frontal sinus embryology.

The fact that the frontal sinus is usually ethmoidal in origin accounts for its frequent intranasal presence at birth, even though it has no external topography at that time.

The painstaking and meticulous anatomical investigations of J. Parsons Schaeffer have elucidated many important structural facts concerning the frontal sinus.

Later Development of Frontal Sinus.—The anlage of the frontal sinus starts to progress in post-fetal life and begins to invade the horizontal (orbital) plate of the frontal bone. It later extends into the vertical plate of the frontal bone. The latter extension tends to occur posteriorly, so that a thin posterior and a thick anterior plate are formed. The posterior plate is thin and made of compact bone, whereas the anterior plate is thick and made of compact and diploetic bone. The frontal sinus is slow in growth until about the age of seven when it begins to increase in size, reaching its full development at about the age of twenty years.

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Read before the Section of Otolaryngology of the College of Physicians of Philadelphia, January 15, 1941.

The Adult Frontal Sinus.—Bilateral symmetry is rare in the frontal sinus. Asymmetry and anatomical variations are the rules rather than the exceptions. Numerical duplications of the sinuses are common, and absence of the sinus is a possibility. Schaeffer has observed four frontal sinuses on each side, each with a separate distinct naso-frontal communication.

It is evident, therefore, that the frontal sinus is a complicated cavern with an especially complicated entrance hall.

The frontal sinus usually occupies portions of the vertical and horizontal plates of the frontal bones. An inter-frontal septum is practically always present but is only rarely in the mid-sagittal plane since the two sinuses are so often asymmetrical. The anterior wall forms the prominent superciliary ridge above the eyebrow. A thick and heavy superciliary ridge does not necessarily imply a deep and large frontal sinus.

Naso-frontal Communications.—The so-called naso-frontal duct is not a simple channel. It is as varied and unusual as the sinus it is supposed to drain. Its anatomical configuration and clinical accessibility and efficiency depend upon its embryological genesis.

A frontal sinus which has developed from the frontal recess will frequently have no true naso-frontal duct. Such a sinus will communicate directly with the adult recessus frontalis in the middle meatus.

A frontal sinus which has developed from the anterior ethmoidal region will more frequently have a naso-frontal duct. Its tortuosity and direction will depend upon the positions of surrounding anterior ethmoidal cells. It may, however, empty into the middle meatus, then into the infundibulum ethmoidale, but such a naso-frontal duct will be contiguous rather than continuous with the infundibulum.

In a dissection of 100 specimens, Kelvin Kasper of Jefferson Medical College demonstrated that the ethmoidal infundibulum and naso-frontal connection are dis-continuous channels anatomically in 62% of cases, are in anatomic contiguity in 34%, and are directly continuous anatomically in only 4%.

Inspection of the ethmoid labyrinth reveals in almost every specimen a rather thin bony roof. It is easy to see how such a thin lamina which forms part of the anterior cranial fossa could be penetrated during the attempted sounding of a frontal sinus, in which there existed a lack of continuity in the naso-frontal connection.

The Frontal Sinus in Children.—As described above, the development of the frontal sinus is slow in early childhood and under the age of seven may be inaccessible from the forehead due to lack of "erosion" of the sinus into the vertical plate. In this instance trephination may be made most feasibly at the T-suture produced by the union of the frontal bone with the nasal bone and the frontal process of the maxilla.

Anomalies in the Frontal Sinus.—As implied above, the anatomy of the frontal sinus consists of a maze of anomalies. The presence of sinus duplications, triplications, and tortuous naso-frontal communications has been described. One must remember that a sinus may extend beyond the midline lying anterior to the opposite sinus, thus producing a false posterior partition.

Partial septa in various planes occur frequently within frontal sinuses. Dehiscences, especially in the orbital plate, are not uncommonly encountered. Frontal inclusions of ethmoidal cells are seen and may complicate a surgical procedure.

Marrow Spaces within the Frontal Bone.—A knowledge of diploetic distribution is of immense importance in prevention and management of osteomyelitis. Obviously enough, osteomyelitis cannot occur in compact bone but requires marrow or diploetic bone. We cannot deny that infection of compact bone may occur, but such an infection is an osteitis and not an osteomyelitis. Osteitis is practically always self-limiting, whereas osteomyelitis is usually a spreading disease. Accordingly, the knowledge of diploetic distribution within the frontal bone is of great surgical importance.

1. The floor of the frontal sinus is almost always compact bone, especially at its inner or medial aspect.

2. The bone of the external or infero-lateral recess or angle of the frontal sinus is highly diploetic. In this area intra-sinus septa are quite frequent, and predispose to obstructive retention with possible osteomyelitis.

3. A dangerous area lies adjacent to the superior sulci of the two frontals where the anterior and posterior plates fuse. This region is highly diploetic and is in contact with the cavity of the sinus as well as with the dura.

4. The anterior plate is almost always diploetic.

Anatomy of the Diploic Veins.—Mosher, Mellinger and more recently, Bucy and Haverfield, have stressed the importance of the

cranial diploic veins in the causation and progression of osteomyeltiis. There are two veins of clinical importance to the frontal sinus, the frontal diploic vein and the anterior temporal diploic vein. They spread upward from the frontal sinus into the diploetic table of the frontal bone to communicate with the superior longitudinal sinus. The frontal diploic vein passes upward from the frontal region about 1 cm. lateral to the midline of the skull. The anterior temporal diploic vein passes upward from the malar region, then curves medially to approach the midline. Bucy and Haverfield contend that thrombophlebitis of these veins precedes osteomyelitis, and have been able to prove the spread of osteomyelitis along the route of these diploic veins both clinically and roentgenologically.

CLINICAL PATHOLOGY

Bacteriology.—Staphylococci are encountered most frequently in both acute and chronic frontal sinusitis and in osteomyelitis of the frontal bone. Some investigators, however, have been able to isolate anerobic nonhemolytic streptococci in the osteomyelitis cases; in these instances the staphylococci are considered secondary invaders.

In an analysis of 18 cases of acute frontal sinusitis in which growths were obtained upon cultures from trephine openings, the following organisms were isolated:

Total number of acute cases trephined		18
Staphylococcus aureus	9	
Staphylococcus aureus hemolyticus	3	
Staphylococcus albus	1	
Total staphylococcic cases		13
Streptococcus—gamma type	1	
Streptococcus—beta type	2	
Streptococcus—viridans type	1	
Diplococcus pneumoniae—type 32	1	

Thirteen out of 18 cases or 72% of the total were due to staphylococci. The cases were from the Departments of Otolaryngology of the Los Angeles County Hospital and the Children's Hospital during the previous twelve months.

Etiological Factors.—Frontal sinusitis usually follows upper respiratory infections. There are, however, certain extrinsic etiological factors, of which swimming and trauma are the most important. Swimming has been responsible for innumerable tragedies arising from the frontal sinus. Infection has occurred in non-divers as well as divers. It seems logical that the tremendous rush of water into the nose during a dive, especially an improperly performed dive, will

cause forced entrance of contaminated fluid into the sinuses. The bad effect of swimming is due to several factors, namely (a) chilling of body surfaces with subsequent lowered tissue resistance, as definitely demonstrated by H. Marshall Taylor; (b) actual contamination of the water by pathogenic organisms; (c) irritant action of chlorine or other disinfectants on nasal mucosa, causing lowered tissue resistance in the nose; (d) displacement of pus from another sinus to the frontal by repeated diving.

Trauma to the frontal region has been reported as a cause of osteomyelitis, especially when trauma is imposed upon a chronic frontal sinusitis. Such trauma may diminish tissue resistance in the bone to the point of inciting spread from an infected mucosa, or in a latent osteomyelitic focus.

Histopathology of Acute Frontal Sinusitis.—The pathology of acute frontal sinusitis is essentially at first a hyperemia and diffuse inflammation of the sinus mucosa with the usual phenomena of serous exudation, polymorphonuclear and lymphocytic infiltration. The dangerous aspect of this pathological process, however, is that the acute exudation of purulent material occurs within a closed bony cavity. The channel of egress, the naso-frontal duct, may become closed or partially closed at this time by intense edema of its mucosa. Accordingly, we may be dealing with a closed abscess cavity. The contained pus and gas formed by bacterial growth produce an increased pressure within this cavity. By virtue of the fact that the frontal sinus is in close proximity to the brain, that a considerable portion of its bony wall is composed of diploetic or marrow spaces, and that a rich diploic venous system drains these spaces towards the meninges and the brain, any increase in pressure within this bony box-like cavity can easily be transmitted to the diploe, the diploic veins, the meninges and the brain.

It is evident, therefore, that unless the intra-sinus pressure is relieved by the institution of adequate drainage, progression of the inflammation must occur. The first process is a retrograde thrombophlebitis from the infected mucosa back to the bone. If this bone be compact an osteitis occurs, if the bone be diploetic an osteomyelitis occurs. Most frequently the thrombophlebitis extends to the dura. In some instances the thrombophlebitic process extends to the periosteum alone, setting up a periostitis.

Osteitis will usually be limited either to the posterior plate or to the floor, and is not a progressive process. It may result in sequestration.

Osteomyelitis frequently involves the anterior plate and the external angle of the frontal bone, in a progressive spreading process traveling upwards through the marrow spaces of the cancellous portion of the frontal bone above the sinus. It rarely occurs without sequestration except in the fulminating fatal variety. The mortality of osteomyelitis of the frontal bone is high even in the so-called non-spreading variety.

DIAGNOSIS

Acute frontal sinusitis is usually ushered in by a fairly sudden onset of pain above the eye. The pain may be accompanied by tenderness, edema and redness of the frontal region. In severe cases the pain is constant. In milder cases with intermittent spontaneous drainage, the pain is characterized by appearing shortly after the patient arises in the morning. The pain then persists until about 4:00 p. m. at which time it begins to decrease and perhaps disappear, only to recur the next morning. Edema of the upper eyelid and injection of the bulbar conjunctiva are often seen. Intranasal findings may be rather meager. The mucosa in the region of the middle meatus may be highly engorged and streaked with pus, or the mucosa may appear relatively normal. A history of preceding upper respiratory infection with or without swimming will usually be obtained. Fever may range from 100 to 105 degrees, and the patient is clinically acutely ill. Transillumination may or may not reveal increased density on the affected side. Similarly it is important to note that X-rays do not always show opacity. X-ray evidence of acute sinusitis is not apparent early enough in the course of the disease to warrant placing upon it any reliance. It is important, however, to obtain an X-ray in order to ascertain the presence of a frontal sinus, and its dimensions.

The diagnosis of acute frontal sinusitis, while usually fairly simple to make, is at times fraught with difficulty. Differential diagnosis from ethmoiditis is not easy, especially where an ethmofrontal cell is involved. In children, the frontal sinus may still be essentially an ethmoid cell. Lid abscesses, orbital abscesses and acute disease of the lacrimal apparatus may simulate frontal sinus disease.

TREATMENT

The patient should be put to bed in a room of warm, even temperature. Shrinkage should be effected by the use of neosynephrine and ephedrine. No hesitation need be felt in the use of adrenalin

1-2000 and cocain 4%. They should be used in the form of pledgets gently insinuated into the middle meatus, after preliminary shrinkage of the nasal mucosa. Ice packs, or heat in the form of compresses, infra-red lights, or diathermy, may be applied to the frontal region, according to the individual response in comfort. Appropriate medication for relief of pain should be administered. Measures to secure proper elimination are routine.

Chemotherapy is indicated especially if a specific bactericidal drug for the particular organism is available; for the staphylococcic group, which is the largest, sulfathiazole or sulfapyridine may prove to be of value.

The persistence of headache, with or without fever, in spite of intensive nasal shrinkage, calls for an early external trephine. The decision as to length of time necessary for a trial with intensive shrinkage before trephining depends upon the judgment of the individual physician. No absolute time limit can be given. Early trephine is indicated if the pain is severe and continuous and is accompanied by fever. Otherwise, the indications for trephine would depend on the degree of intermittent pain, leucocytosis, fever, or other symptoms pointing to marked stasis and interference with drainage. Under no circumstances is it safe or advisable to attempt any intra-nasal instrumentation except the placing of pledgets as described. Intranasal surgery is to be condemned in acute processes. The use of the rasp or curet, or amputation of the anterior tip of the middle turbinate is highly dangerous. Such mucosal trauma will invite rapid thrombophlebitic spread of infection to the meninges and marrow spaces. Probing and cannulization of an acutely inflamed frontal sinus is dangerous. Kasper showed that in 66% of cases the fronto-nasal duct had no continuity.

In swimmers, the incidence of osteomyelitis and other severe complications has been so great, that unless adequate drainage from the frontal sinus is established at once with immediate relief of symptoms, trephination is indicated as an emergency procedure.

It is far safer to go through the compact non-marrow-containing bone at the medial aspect of the floor of the frontal sinus and establish adequate dependent external drainage. If a subperiosteal or orbital abscess is seen at the start, one should do an immediate external trephine without any attempt at intensive nasal shrinkage.

The trephine may be made in the following manner. Preliminary X-rays should be available as anatomic guides to the extent

of the sinus. Under general anesthesia an incision is made below the medial portion of the eyebrow at the inner angle of the frontal bone. The eyelids should be sutured together. The incision is made to the bone and the periosteum elevated carefully for a very limited area so that at the end of the trephine no bone will be left uncovered by periosteum. Trephination may be done at the medial aspect of the floor of the frontal sinus close to the junction with the anterior plate. The hole should be large enough to admit a fairly rigid rubber tube with an inner lumen of not less than 8 mm. No attempt is made to touch the mucosa; free pus is gently aspirated and the tube inserted and sutured in place to the skin. The lid suture is removed.

After the acute process subsides and purulent drainage ceases, the tube is withdrawn and the wound allowed to close. The resulting scar is negligible and constitutes no cosmetic hazard.

COMPLICATIONS

1. *Meningitis.*—Meningitis as a complication of frontal sinusitis is much less common than otogenic meningitis. The onset of meningitis due to frontal sinusitis is characterized by the usual signs of meningeal irritation—irritability, nuchal rigidity, hyperactive deep reflexes, pathological reflexes and characteristic spinal fluid changes.

The appearance of meningeal signs in the course of an acute frontal sinusitis indicates that a retrograde infection has taken place. Such retrogression may occur in one of four ways:

a. By thrombophlebitis invasion of the meninges through the cranial diploic venous system.

b. By direct extension through an osteitis of the posterior plate.

c. Through extension from an extradural abscess.

d. Following osteomyelitis.

Signs of meningeal irritation in the absence of osteomyelitis call for immediate removal of the posterior plate of the infected frontal sinus by enlarging the trephine opening sufficiently to deal adequately with the posterior plate. In the case where meningeal signs are due to osteomyelitis, more extensive surgery to remove the osteomyelitic bone is indicated.

If the meningitis is due to an extradural abscess, posterior plate removal may be sufficient to permit adequate drainage of the extradural abscess, and check the localized meningitis.

2. *Periostitis and Sub-periosteal Abscess.*—As Mosher has demonstrated, venous extension may occur not only to the meninges but also anteriorly to the periosteum overlying the frontal sinus. It is, therefore, possible for a periostitis to develop following either osteitis or osteomyelitis. The location of periostitis with or without subperiosteal abscess is of great prognostic importance. A subperiosteal abscess below the eyebrow may be due either to osteitis of the floor of the frontal sinus or to periostitis from the lamina papyracea from a concomitant ethmoiditis which almost always accompanies frontal sinusitis.

If the sub-periosteal abscess occurs above the eyebrow it should be considered as due to osteomyelitis unless proven otherwise. Accordingly, a sub-periosteal abscess below the eyebrow offers a much better prognosis than one above the eyebrow.

3. *Osteomyelitis.*—It is not within the province of this paper to discuss at great length the problem of osteomyelitis of the frontal bone. This disease, however, does loom as probably the greatest menace in infections of the frontal sinus.

Differences of opinion as to "radical" and "conservative" surgery in this disease are legion. Most rhinologists now agree, however, that if a given case be definitely established as "localized" osteomyelitis, local drainage and later removal of bone sequestra during the quiescent stage are indicated. They also agree with considerable unanimity that in a definitely established "progressive" or "spreading" osteomyelitis, a radical immediate removal of all diseased bone including one and one-half to two inches of the surrounding normal bone is indicated. The great and frequently insurmountable difficulty confronting the rhinologist is to differentiate between the "localized" and "spreading" varieties. X-ray evidence of osteomyelitis lags behind the clinical course by days or weeks.

4. *Longitudinal Sinus Thrombosis.*—The longitudinal cranial venous sinus occasionally is involved by thrombophlebitis of the diploic veins arising in an acute frontal sinus, or more frequently from an acute osteomyelitis of the frontal bone. This is a serious complication and is seen usually in terminal cases.

5. *Extra-dural Abscess.*—The removal of the posterior plate for meningeal signs or for osteomyelitis will not infequently disclose an extra-dural abscess. Persistent frontal pain after adequate drainage, in the absence of demonstrable osteomyelitis with or without signs of increased intra-cranial pressure, points to a possible extra-dural

abscess or true brain abscess. In this instance, removal of the posterior plate is to be urged in order to uncover a possible extra-dural abscess.

6. *Intra-cerebral Abscess.*—True brain abscess is a rather frequent sequel of osteomyelitis of the frontal bone and is less often the result of acute frontal sinusitis. It is not uncommon to see a patient who has apparently recovered from an osteomyelitis process suddenly succumb to the rupture of an undiagnosed brain abscess into one of the ventricles. The latent period in the development of an intracerebral abscess should always be considered. Whereas frontal lobe abscess is the most common type associated with this disease, abscesses in the temporal, parietal and cerebellar regions have been encountered by the writer.

The diagnosis of frontal lobe abscess is one of the most difficult in neurology. Classical signs of increased intracranial pressure occur only late or not at all in the course of a frontal lobe abscess. Personality changes may be noticed in frontal lobe pathology. The transmission of infection from the frontal sinus or from osteomyelitis of the frontal bone through venous channels of the diploic and superior longitudinal veins can account for retrograde infections resulting in either contra lateral or ipsi lateral cerebral abscess formation.

CHRONIC FRONTAL SINUSITIS

The development of chronic frontal sinusitis is usually due to repeated attacks of the acute process. Occasionally, however, it may be due to a single acute attack, in which anatomical factors prevent a complete recovery. It is, therefore, of the utmost importance to follow carefully each acute case until complete recovery is assured. The most important etiological factor, however, may be an anatomic obstruction preventing proper drainage and ventilation.

PATHOLOGY

Recurrent acute attacks and mechanical or pathological obstructions to adequate intranasal drainage of the frontal sinus predispose to chronic infections. In many cases an associated ethmoiditis or maxillary sinusitis is present, and contributes to the etiology and persistence of the frontal sinusitis. Pathologically, the normally thin mucosa becomes markedly thickened with monocytic and eosinophilic infiltration. The epithelium undergoes cloudy degeneration and may become entirely necrotic. An intense vascular congestion

is sometimes apparent. Hyperplastic and cystic degeneration is commonly found and the hyperplastic process may lead to polyposis. The cystic degeneration may continue to the formation of either mucocele or pyocele. Combinations of suppuration and polyposis are frequently found. The bone may be involved by a chronic sclerosing osteitis with occasional formation of hyper-ostoses. The intersinus septum is often diseased, and the opposite sinus frequently involved by extension.

Allergy of the nasal mucosa may play a very dominant part in the etiology, recurrence and progression of a chronic frontal sinusitis. It may do so by the formation of polypi in the anterior ethmoid cells, thus obstructing drainage and ventilation of the frontal sinus.

DIAGNOSIS

The most common complaint is unilateral frontal headache, usually intermittent in character and accompanied by tenderness on palpation or percussion. The patient may complain of photophobia, lack of ability to concentrate, and purulent nasal discharge. The pain and tenderness are indicative of inadequate drainage. The pain begins shortly after arising in the morning and increases in intensity for four to six hours, when relief is experienced, usually coincident with discharge from the sinus. Apparently postural change facilitates drainage and alleviates pain.

Transillumination will usually show an opaque frontal sinus on the affected side. X-ray examination will show increased density and mucosal thickening in the affected frontal sinus. Intranasal examination will show in most cases a discharge of pus in the middle meatus.

TREATMENT

The general health of the patient should receive just consideration. Constitutional diseases, as well as dietary, endocrine, and allergic defects, must be remedied. Diseased tonsils and adenoids should be removed. These measures will tend to decrease the incidence of repeated upper respiratory infections. Diseases of the other sinuses should be cleared up before attacking the frontal sinus, since experience has shown that many frontals successfully clear up when such steps are taken. Proper treatment of the inferior sinuses will frequently secure better drainage from the frontal sinuses by clearing the inferior aspect of the fronto-nasal duct.

Intranasal Treatment.—The nose should be carefully surveyed for eradicable, obstructing anatomic or pathologic structures, which prevent drainage from the frontal sinus. Evident septal obstruction, especially high, should be removed by submucous resection.

In the absence of fistulae and other complications, an intranasal procedure is justifiable as a preliminary attempt to deal with a chronic frontal sinusitis. Ethmoiditis is so frequent in frontal sinus disease that it would be rare to find a normal ethmoid in the face of long continued purulent discharge from the frontal sinus. Therefore, whether the obstruction be anatomical or pathological or both, we believe that the anterior ethmoids should be properly exenterated as a preliminary step in the treatment of frontal sinusitis. Such a procedure is best exemplified by a partial, anterior, middle turbinectomy and an anterior ethmoidectomy of the Mosher type. The use of the rasp has not been found worthwhile, and on the contrary is probably responsible for postoperative stenosis of the naso-frontal passageway, by stimulating new bone formation. The intranasal operation should endeavor merely to remove anatomical or pathological obstruction at the inferior aspect of the naso-frontal passageway.

External Surgery.—Unsuccessful intranasal surgery calls for an external operation. Symptoms of retention manifested by persistent headache and pain require external surgery. An external fistula cannot be dealt with satisfactorily except by external surgery. In general, there are two types of external operations on the frontal sinus. The first, described by Lynch and modified by Sewall, is a conservative approach through the floor of the frontal sinus, leaving the anterior wall intact. The second operation advocated by Killian is a radical obliterative operation in which the floor and the anterior plate are removed.

Lillie has very clearly stated the indications for both procedures. According to him, the Killian operation is necessary in cases with necrotic or diseased anterior plates. It is also indicated in a large multilocular sinus with a short antero-posterior diameter. Such a sinus could not be satisfactorily approached by merely removing the floor, as its mucosa could not be thoroughly removed.

The Lynch or Sewall operation, or some modification thereon, is used most frequently. It is a conservative approach which is not deforming, yet offers adequate exposure in the majority of cases. Incision is made immediately below the unshaven eyebrow. The periosteum is elevated inferiorly, but is untouched superiorly because if so done it is unlikely to reapply itself and may cause subsequent

death of underlying bone with all of the serious sequelae that accompany sequestration in osteomyelitis. In general, the operator should be careful to leave no bone uncovered by periosteum.

The bone work consists of removal of the floor of the frontal sinus along with part of the antero-medial orbital wall. The anterior plate and superior orbital ridge are left intact usually, thus insuring no significant cosmetic defect. Exenteration of infected ethmoid cells adjacent to the frontal sinus and fronto-nasal duct is done at the same time if not done previously. Success of the external approach depends largely upon meticulous attention to detail in the operative technique. The purpose of the operation is to remove every vestige of infected mucosa from the walls of the sinus. No hidden corner should go untouched. A frequent cause of failure is lack of removal of infected membrane in the infero-lateral crevices of the sinus.

A very important aspect of the operation is the treatment of the naso-frontal duct or passageway. Upon this feature more than any other depends the final success of the operation. The lamina papyracea may either be removed partially or completely, depending upon the anatomy of the nose. If the nose is a wide one, the lamina may be removed fairly completely in order to allow the orbital contents to bulge medially into the nose and thus prevent atrophic nasal changes. If the nose is a narrow one, the lamina may be allowed to remain partially, in order to prevent prolapse of orbital contents into an already narrowed fronto-nasal channel.

Lillie emphasizes the importance of not removing the frontal process of the superior maxilla. If it is left in place it will help maintain the patency of the fronto-nasal duct. The placing of grafts within the naso-frontal communication to insure patency of the lumen has been urged by Smith and others. Skin grafts have been tried frequently but have not been too satisfactory.

Mucosal grafts as advocated by Sewall are of distinct advantage. Such grafts may be taken from the lateral nasal wall anterior to the turbinates or from the nasal septum. If a graft is not used, a good-sized firm rubber tube is left in place, from the frontal sinus to the nose for at least two weeks, during which time it should be kept patent. This is usually sufficient to insure epithelization.

An important precaution in placing such a tube is to avoid having the upper part of the tube project into the sinus. It should be flush with the floor to prevent stagnation of secretions within the sinus.

Lillie uses the funnel-shaped mouth of a catheter at the floor of the sinus instead of an ordinary tube. This undoubtedly helps to maintain the patency of the upper part of the naso-frontal duct, and if left in place for two weeks will probably permit epithelization with or without graft. Lynch warned against placing sutures through the periosteum of the upper part of the wound during the closure in order to prevent any elevation of the periosteum.

Experience with the Lynch operation has demonstrated that it causes no disagreeable crusting or surgical atrophic rhinitis unless the anterior sphenoidal wall is removed.

The indications for the obliterative or Killian type of operation have been given above. The frequent objection raised in regard to cosmetic difficulty may be remedied by a careful beveling of the superior sulcus of the frontal sinus plate so that no prominent hump remains at the junction of the anterior plate with the frontal bone proper. This technique was first advocated by Lillie and has proven successful in his hands.

One must always remember that a seemingly unilateral frontal sinusitis may have an infected quiet partner lurking on the other side of the interfrontal septum. To leave such a silent partner alone is to invite failure of operative procedures.

Summary of Indications for Surgery in Acute Frontal Sinusitis:

a. External trephine is an emergency measure in swimmers who do not obtain prompt relief by shrinkage.

b. External trephine is indicated in sub-periosteal abscess below the eyebrow.

c. Removal of the posterior plate is indicated in either meningitis or symptoms of extra-dural abscess.

d. Prompt radical removal of diseased bone is indicated in spreading osteomyelitis.

e. Intranasal surgery is to be condemned in acute frontal sinusitis.

Summary of Management of Chronic Frontal Sinusitis:

a. Systemic treatment including allergic endocrine and dietary management.

b. Submucous resection for septal obstruction.

c. Removal of diseased tonsil and adenoid tissue.

d. Correction of suppurative disease of other paranasal sinuses.

e. Preliminary anterior ethmoidectomy intranasally. (Mosher.)

f. External surgery indicated if previous measures unsuccessful.

1. Fistula calls for external surgery.

2. Symptoms of retention call for external surgery.

3. Lynch or Sewall procedure adequate for most cases.

4. Killian obliterative operation necessary for disease of external table and for multilocular sinuses with small A-P diameter.

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XXX

OSTEOMA OF THE FRONTAL SINUS*

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Osteomata occurring in the nasal accessory sinuses are uncommon, although they are encountered occasionally in any large hospital service. They are found more frequently in the frontal sinuses than in any of the others and may arise from either the anterior or posterior sinus walls, although more commonly from the former. Frontal sinus osteomata are, fortunately, more often pedunculated than sessile and may be grouped roughly into two classes according to their consistency—hard and soft. The first named variety is compact bone, ivory-like or sclerotic in character, while the latter is of softer bone, even approaching the cancellous type. There are also, of course, growths whose structure is in between these two extremes. They are of slow growth as a rule, causing no symptoms in the early stages, during which they may only be discovered by accident as when X-raying or operating upon a frontal sinus for infection. The infection may, indeed, have been caused by the tumor if its location was such as to obstruct drainage and ventilation of the cavity. In uninfected cases, the gradual development of headache, caused by growing pressure of the neoplasms, is often the first signs of its presence, but headache may be absent until increased growth makes pressure upon an adjacent wall or structure. If the growth extends inward, the dural plate of the sinus may become absorbed with the production of neurological symptoms. More commonly growth is in the outward or downward direction resulting in a protruding deformity over the eyebrows or a projection into the orbit through the thin orbital roof, with displacement of the eyeball and limitation of its motion. Eventually, loss of vision would occur unless the condition was remedied by appropriate surgery. In either case, the bony wall upon which the tumor encroaches may be reduced to paper thinness or entirely absorbed so that the growth lies under the peri-

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osteum of the frontal plate or within the orbit pushing the periorbita ahead of it. Frequently there is a history of trauma elicited, but whether this is a definite etiological factor is not known. It may be that trauma plays a part in some cases, as suggested by Barnes, by activating some quiescent congenital fault, and infection may play a similar role. It seems more likely, however, that when infection is present it is secondary to the deformity caused within the sinus by the obstructing neoplasm. The diagnosis rests upon the external deformity, which at times is the only symptom complained of, the pain, invasion of the orbit or brain cavity and confirmatory roentgen ray examination. The only confusion likely to occur is the differential diagnosis between osteoma and the osteogenesis described by Skillern. Growth, while usually gradual and progressive, may become stationary before causing enough symptoms to call for detailed examination.

The treatment is entirely surgical as soon as there are enough symptoms to warrant a diagnosis and removal. The external plate of the frontal sinus is removed as for any exposure of the sinus for other reasons, and if the tumor has a definite pedicle and is of the hard or compact variety, it can be removed without much difficulty with the chisel. If it is sessile, however, a different problem is presented as the chisel cannot be used to separate it from the bone from which it grows and of which it is an integral part, without danger of fracture and injury of important ocular or intracranial structures. This point will appear in the detail of the two cases reported herewith.

The two cases upon which this report is based are presented because both were seen within a short time of each other, both occurred within the first three decades of life, in which osteoma is most commonly discovered; each had large, well developed frontal sinuses, in each of which the inter-sinus septum had been destroyed; each produced marked external deformity; in each the tumor was of the compact variety, sessile and an integral part of the internal table; each osteoma was very large in size, almost completely filling both frontal sinuses; in each the anterior table had been reduced to tissue paper thinness (in one the table was completely absorbed over a considerable area); and in neither case was there any evidence of sinus infection. In the second case, perforation into the orbit had occurred. The procedure of removal was identical in each case except that in the second the supra-orbital ridge was an integral part of the tumor or had been absorbed by it and, therefore, was removed, as it happened, with little deformity. In each, convalescence was rapid and uneventful, and, possibly because bone chips were implanted

Fig. 1. Case II, before operation.

Fig. 2. Case II, after operation.

Fig. 3. Case I.

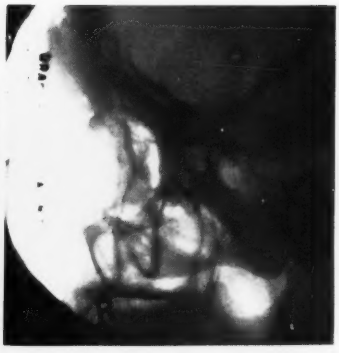

Fig. 4. Case I.

upon the exposed dura, almost complete regeneration of bone covering the dura took place rapidly.

REPORT OF CASES

CASE I.—R. deR., aged 25, a miner, male, white, was admitted to the Graduate Hospital of the University of Pennsylvania on April 26, 1939, his chief complaint being a "lump on his forehead."

The history of this dated back seven years, when he noted a pea-sized lump over his glabella. This had never been painful, tender or sensitive to touch. It always seemed firm and hard, and it gradually increased in size until it formed a marked bony prominence and deformity on the forehead. Throughout this period, until recently, there were never any symptoms associated with the increase in size of this mass. About two months prior to admission, however, he began to notice a dully aching pain in the frontal region. This was not constant, and it was always of the same intensity. His chief consideration was the deformity.

The past medical history was irrelevant. There had been no nasal operations or symptoms of sinus infection. There was no history of trauma obtainable. Patient was a moderate to hard drinker and smoked to excess. The physical examination was essentially negative, except for the deformity. This appeared as a hard bony protuberance, about 3 cm. in diameter, very firm, without any pain or tenderness on pressure. After admission, the X-ray examination revealed "a large dense mass, probably an osteoma, extending from the posterior plate of the frontal sinus and completely filling both sinuses." This was present in the midline and measured 5 cm. by 3.5 cm. The anterior wall of the frontal sinuses bulged forward, was very thin and was entirely missing in an area about 1 cm. in diameter. The ethmoid sinuses showed a slight clouding on the left. The maxillaries were negative, but the left sphenoid sinus showed a slight thickening of the mucous membrane. The routine laboratory studies were normal in every respect. Eye examination was negative. There was moderate hyperostosis of both external auditory canals.

On April 28, 1939, two days after admission, under avertin anesthesia, an external frontal sinus operation was performed. A hard bony mass was found attached to and an integral part of the posterior wall of the sinus from which it originated; this measured 5 cm. in width, 4 cm. in height and 3 cm. in thickness. The mass, with the posterior wall of the sinuses, was removed. The anterior walls of both frontal sinuses were reduced to tissue paper thinness, were entirely missing in the midline and were bulging forward mark-

edly. The inter-sinus septum had been destroyed as had also been the roof of the right orbit. The left orbital roof was very thin. The right superciliary ridge had been largely absorbed, while the dense bony growth, filling practically the entire cavities of both frontal sinuses, which were large, arose from and was continuous with the entire posterior sinus wall. As it was impossible to separate the growth from this wall due to its ivory-like consistency, the entire dural plate of the sinuses with the overlying osteoma was removed in one mass by the use of angular V-shaped chisels. No laceration of the dura occurred. The pathological report was osteoma originating from the posterior wall of the frontal sinuses, sessile, compact variety. As it was also necessary to remove the superior portion of the orbital plate, the attachment of the superior oblique muscle was loosened. No infection was found in the sinuses. Both naso-frontal ducts were packed to prevent the entrance of infection from the nose, the exposed dura was sprinkled with bone chips, taken from the edges of the frontal bone, and the skin flaps then sutured with rubber tissue drains in the outer angles of the incision.

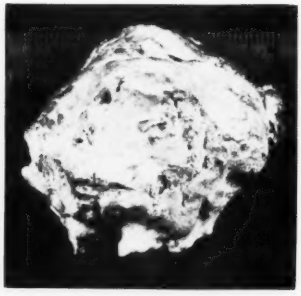

Fig. 5. Case I.

For several days following the operation, there was a slight elevation of temperature. On the fourth postoperative day, May 2, 1939, the wound was revised, the drains and the packing in the naso-frontal ducts were removed, the dura again sprinkled with bone chips and the wound was again closed. Routine postoperative care was supplemented with sulfanilamide therapy as prophylaxis against infection. The temperature quickly dropped to normal, and convalescence was uneventful throughout the rest of the stay in the hospital. There was no diplopia following the operation. A culture report on the frontal sinus revealed Staphylococcus albus hemolyticus, probably a contamination. The patient was discharged on May 11, 1939, in good condition, to return to his private physician. He was next seen on August 7, 1939. He had experienced only slight headache, the depression over the frontal sinus area was rapidly filling in, and there was little deformity. There was no sign of recurrence, and bony regeneration of the dural plate was definitely progressing. The last time this patient reported, in July, 1940, the posterior wall of the frontal sinuses had entirely regenerated.

CASE II.—L. C., aged 15 years, while playing football, was hit over the right eye on May 28, 1939. He had a severe headache lasting two weeks. The lids of the right eye were ecchymosed and swollen, but this subsided in two weeks. Six weeks later, the right upper lid began to droop and the headaches returned in greater severity, much worse at night or after use of his eyes.

On October 5, 1939, he came to the eye clinic of the Abington Memorial Hospital. There was present a ptosis of the right upper lid of about 4 mm. The eye grounds were normal. The vision in the right eye was 20 30+ and in the left eye 20 20. A break in the contour of the right orbital ridge was found and X-rays immediately ordered. These films showed no line of fracture, but did show a somewhat irregularly shaped abnormal shadow completely filling the right frontal sinus. The density of the shadow was much greater than the surrounding bone and extended slightly beyond the midline.

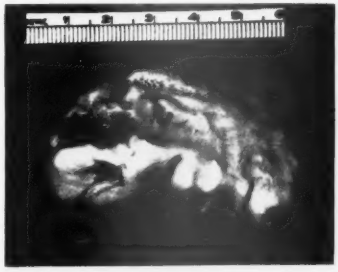

Fig. 6. Case II.

The patient was referred to the nose and throat clinic on October 20, 1939, when the nose and throat were found to be normal with no nasal discharge found nor complained of by the patient.

The ocular symptoms increased. The ptosis was more marked, with gradual displacement of the eyeball downward and outward and much proptosis. An X-ray examination on March 19, 1940, showed an increase in the abnormal shadow in the frontal sinus with extension through the roof of the orbit.

It was evident that the tumor was rapidly progressing in size. The anterior wall of the right frontal sinus was pushed forward and outward. The headaches were intense. The patient became irri-

Fig. 7. Case II.

Fig. 8. Case II.

table and easily fatigued and the mental processes much dulled. He had had no fainting attacks. The olfactory sense remained normal.

The personal history had no apparent significance. Tonsillectomy was done in 1930. He had had pneumonia eight years previously, but none of the contagious diseases of childhood. The parents were living and well. There is a history of cancer in the father's family.

The patient was admitted to the Abington Memorial Hospital on April 22, 1940, and operated upon next day under avertin and ether anesthesia. After preparation, the incision was made in the line of the right eyebrow following the orbital ridge along the side of the nose to the level of the caruncle. From there a horizontal cut was made over the nasal bones to the opposite side, the incision carried to the forehead and extended through the brow line on the left side. In this way a large flap could readily be held out of the way, exposing the frontal bone. The anterior wall of the frontal sinus was reduced to tissue paper thinness. This was removed, exposing a large white tumor which was very hard and adherent to the surrounding bone. It completely filled the lumen of both frontal sinuses, the inter-sinus septum having been absorbed. It was necessary to remove the inner half of the orbital ridge on the right side as this was an integral part of the osteoma. The tumor was removed in its entirety together with the inner plate of the skull, which could not be differentiated from the osteoma. This was done with the chisel and exposed a large area of dura, which was not injured. No infection was present. The roof of the right orbit was similarly

affected. The wound was closed with small rubber drains in the outer aspects of the wound.

Healing was by first intention. The eyeball returned to its normal position with no diplopia, no recession of the ball and no ptosis. The headache and other symptoms have disappeared. The X-ray shows complete removal of the tumor. The neurological examination is negative.

The tumor was densely white and very hard. It measured 6 cm. long and was irregularly shaped, varying in diameter from 3.2 mm. to 2 cm. The specimen was flattened. The posterior surface showed a section of flat bone firmly adherent to the overlying osseous tumor. A section of the specimen was soaked in nitric acid for six weeks before decalcification took place. The diagnosis, pathologically, was compact sessile osteoma.

At the present writing, November 26, 1940, the patient is well, shows little deformity aside from a moderate flattening of the right supra-orbital ridge, and the bony defect in the skull has been completely closed by osteogenesis.

In reviewing this history, it seems improbable that a growth as hard as this could grow to such a size within one year. A decided increase in the growth is noted between October 29th and the following March, with evident absorption by pressure of the walls of the frontal sinus—all of them being paper thin and adherent to the growth. The absence of purulent or other discharge indicates a sterile tumor, an utter absence of bacterial origin. A point of interest here is the rapidity with which this osteoma grew during the short space of one year, while under observation.

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XXXI

A BROADER CONCEPT OF FUNCTIONAL DISEASES OF THE NOSE

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A proper understanding of this subject is possible only if one recognizes the relationship between the function of the nasal mucous membrane and the functions of the nose itself.

Briefly, the function of a mucous membrane is to produce mucus, but the nasal mucous membrane must produce mucus within certain quantitative limits if the nasal functions are to be perfectly maintained. Any shifting of this mucus production into either a hypofunction or a hyperfunction will result in a functional nasal disturbance, and the signs and symptoms of this disturbance will depend upon the amount and character of the dysfunction and the length of time it has continued.

:	Hypo-function	:	Normal function	:	Hyper-function	:
A		B		C		D

(Fig. 1.)

In terms of the diagram (Fig. 1), so long as the amount of mucus secretion remains within the normal zone B-C, other things being equal, the functions of the nose will be normal. If, however, the amount of secretion shifts into zone A-B (the hypofunction area) or into zone C-D (the hyperfunction area), a functional disease of the nose will result, and its severity will depend upon how far either right or left the diagrammatic shuttle moves.

The olfactory, respiratory, humidifying, and ciliary functions of the nose, like other physiological processes, are carried on only in the presence of a proper amount of fluid. A dry nasal membrane loses its humidifying properties and sense of respiration; its cilia become sluggish; and if the dryness is long continued, the sense of smell is impaired and atrophy results. On the other hand, an overwet nasal membrane obstructs the respiration, diminishes the sense

of smell, produces pressure symptoms, and if long continued, develops a hyperplasia.

Functional diseases of the nose result when an improper production of mucus occurs. Years ago, the terms "dry catarrh" and "wet catarrh" were entities. Now we know that nasal hypofunction and hyperfunction are reactions from definite causes, and that proper treatment implies an understanding of these causes.

We shall now consider the reactions and some of their causative factors.

Hypofunction	Normal Function	Hyperfunction
1. Atropine Rhinitis		1. Irritative Rhinitis
2. Physical Rhinitis		2. Infective Rhinitis
3. Psychic Rhinitis		3. Allergic Rhinitis
4. Atrophic Rhinitis Syndrome:		4. Miscellaneous Types:
a. Rhinitis Sicca		a. Physical Rhinitis
b. Atrophic Rhinitis		b. Psychic Rhinitis
c. Ozena		c. Food Rhinitis
5. Febrile Rhinitis		d. Endocrine Rhinitis
6. Debilitative Rhinitis		e. Others

(Fig. 2.)

HYPOFUNCTION

1. *Atropine Rhinitis:* Atropine, in adequate amounts, always retards the production of mucus. In atropinized individuals, a normally functioning nasal membrane may hypofunction and a hyperfunctioning membrane may function normally or even hypofunction.

2. *Physical Rhinitis:* Warm air, improperly moistened, or desiccating gases, invariably produce a hypofunctioning nasal membrane.

3. *Psychic Rhinitis:* An individual before an audience or microphone often develops a hypofunction of the membranes of both the nose and throat. The speaker's glass of water is handy not because he is thirsty but because his membranes get dry.

4. *Atrophic Rhinitis Syndrome:* This is an organic condition producing a functional nasal disturbance. It begins as a simple rhinitis sicca, passes into an atrophic rhinitis, and often terminates in a

putrefying oezena. Perhaps this is a Reynaud's disease of the nose. In any case, it manifests itself as a progressive, permanent vasoconstriction, an impairment of secretory and ciliary action, and often a partial or complete loss of all nasal functions.

5. *Febrile Rhinitis:* The dry, scabby nasal membranes associated with febrile diseases are always the result of nasal membrane hypofunction.

6. *Debilitative Rhinitis:* This condition illustrates the interdependence of bodily functions. A debilitated body can be responsible for nasal mucous membrane languor. Advanced cardionephritics often have an oezena type of rhinitis; chronic invalids frequently acquire atrophic rhinitis; and even sedentary individuals are subject to recurrent or persistent attacks of rhinitis sicca.

HYPERFUNCTION

1. *Irritative Rhinitis:* Onion, ammonia, and various other fumes and gases cause an immediate nasal hyperfunction. Exposure to small amounts of irritating agents over an extended period of time results in a long continuing (not necessarily chronic) hyperfunction.

2. *Infective Rhinitis:* The "common cold" with its complicating sinusitis, probably bacterial in origin, is the most common of the hyperfunctioning diseases.

3. *Allergic Rhinitis:* Differing from the infective rhinitis in that its swelling is extra-capillary rather than intra-capillary (that is, the mucous membrane is pale rather than red), this is probably the second most common functional disease of the nose.

4. *Miscellaneous Types of Rhinitis:* Many of the hyperfunctioning diseases of the nose are little understood, often undiagnosed, and controversial. To disown or fail to acknowledge this group of functional diseases is to misdiagnose and improperly treat many unsuspecting individuals.

Some physicians classify all discharging noses into one or more of three groups, namely, "colds," sinus infections, and allergies. As a result of this, some noses have had prolonged and ineffectual treatment, and others have had unnecessary surgical manipulations.

The following are some of the common miscellaneous types of hyperfunction:

a. *Physical Rhinitis:* The individual who develops a "cold" when he goes out of doors or when he comes indoors and has

no difficulty at other times, does not have a "cold." His membranes are hyperfunctioning in response to physical agents.

b. *Psychic Rhinitis:* It has already been stated that there can be a psychic nasal hypofunction. Similarly, anxiety or emotion may produce a hyperfunction.

EXAMPLES

(1) A woman, two days before she was to appear in court, developed a bad "cold." One hour after she had testified, the "cold" disappeared.

(2) Another woman with recurrent attacks of anxiety neuroses had "colds" during each attack and was entirely free during the intervals.

(3) A man subject to fits of anger always developed a marked rhinorrhea and salivation during the attack. Both disappeared as the emotion passed.

c. *Food Rhinitis:* Apparently some nasal membranes hyperfunction because of the continued ingestion of certain foods that do not produce a typical allergic rhinitis. D. C. Jarvis has written much on this subject.

(1) *Starches:* White bread and white potatoes are common offenders and in many instances cause a mucopurulent discharge like a chronic purulent rhinitis or a sinusitis. Such a condition may last for months or years. Elimination of the offending food often corrects the functional disturbance, even after a secondary sinusitis has developed.

(2) *Sugar:* "Candy addicts" are often susceptible to "colds."

EXAMPLE

A girl, aged 9, was brought into the office because of a nasal discharge which she had had since three years of age. She had been treated by a competent laryngologist; the tonsils and adenoids had been removed; antrum windows had been made; and local treatments had been given regularly for six years. But at the time of this examination the nasal discharge was purulent and copious. Detection of the cause of the difficulty and elimination of candy from her diet resulted in complete relief of the symptoms, and the patient has been well for eight years.

d. *Endocrine Rhinitis:* The endocrine system also has its effect on the nasal mucous membrane.

EXAMPLES

(1) A girl, aged 15, had a "cold" at every menstrual period for two years. All the common prophylactic measures were used but did not improve her condition. Perhaps she would have improved spontaneously in time, but frequent use of an estrogenic substance gave her complete relief.

(2) A woman, aged 22, had "colds" concurrently with certain pelvic symptoms. These continued for about a year and a half. After removal of a pelvic tumor, the "colds" did not recur.

Many other types could be added to this miscellaneous group of hyperfunctioning nasal membranes, but these give some idea of the diversity and multiplicity of factors involved in hyperfunction.

CONCLUSIONS

1. The nose functions normally only when the nasal mucous membrane functions normally.

2. A normally functioning nasal mucous membrane produces a limited amount of mucus. It does not hypofunction nor hyperfunction.

3. Any hypofunction or hyperfunction of the nasal mucous membrane expresses itself as a functional disease of the nose.

4. Hypofunctional diseases begin with dryness of the mucous membrane, and if long continued terminate in atrophy.

5. Hyperfunctioning diseases begin with engorgement and rhinorrhea, and if long continued terminate in hyperplasia.

6. Relatively few agents or conditions produce hypofunctioning diseases, but many produce hyperfunctioning diseases.

7. It is important to realize that hyperfunctioning diseases are not limited to infective rhinitis, sinusitis, or allergy, but have a vast number of causes.

8. Investigation into these causes, many of which are unusual, will lead to better diagnosis and more efficient treatment.

277 ALEXANDER STREET.

XXXII

SURGERY OF THE NASAL SINUSES*

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SAN FRANCISCO

Why is operative cure of infected sinuses so hard to attain? The answer seems to lie in the difficulty of applying in their treatment well understood surgical principles. These tenets require the obliteration of an infected space. Empyema of the chest, for example, baffled surgeons until rib removal permitted a curative collapse of the cavity. In sinus surgery we are dealing with firm-walled cavities. It is seldom desirable and not always possible to obliterate them. When obliteration is necessitated by the severity of the disease and can, in view of the anatomical structure, be accomplished, a cure, definite and permanent, results. This proves that sinus infection can be surgically cured.

There are in principle two types of surgical management. In the one the cavity is denuded of mucosa, which is replaced by other tissue. Obliteration of the frontal sinus falls under this head. In the other the sinus is made incapable of holding any secretion though what walls remain may be lined by mucosa and exposed to the air. Handling of the sphenoid falls into this category. Removal of its floor robs it of retentive capacity. We may call this "elimination of the sinus" as such. Either "obliteration" or "elimination" should satisfy the surgical demands for cure.

Treatment of the ethmoid cells includes both types of effacement. (1) The orbital extensions are denuded of mucosa and become filled by other soft tissue. (2) The truly intranasal ethmoid masses lose all walls except the roof.

The usefulness of surgical drainage of the sinuses is necessarily in proportion to its efficiency and to the moderation of the infection. In mild cases more or less imperfect drainage may suffice to give clinical relief and at times a cure. These casual surgical measures have been widely used and advocated as of value in "aerating" the cavities. As gravity, unimpeded, does not come into play, drainage

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of such type is of limited value. The cilia become practically helpless in the propulsion of thick discharge. It must at least be granted that cases suitable for such measures have been badly chosen. This is conclusively attested by an aroused public opinion. As the severity of the disease process increases, the demands upon drainage are proportionately enlarged. In the face of excessive changes or unusual healing demands, only ideal drainage will suffice. Such ideal drainage may be impossible to attain. It requires nothing short of the removal of the floor of the sinus so that the cavity may be compared to a tea-cup that has been turned upside down. In the sinus itself everything that in any way interferes with the exit of discharge must be eliminated. Sometimes these obstructive conditions in the sinus, when caused by diseased changes in the lining, will eliminate themselves to a degree when removal of the sinus floor allows gravity full play in the disposal of discharge.

With this review of principles let us examine our surgical procedures and see how they measure up to the necessities here laid down.

For operative purposes the sinuses divide themselves naturally into two groups. The upper comprises the frontal, the ethmoids and the sphenoids. The lower comprises only the antra. When both are diseased it is rarely curative to attack the upper group without attending to the lower and vice versa. It is even necessary to combine work on both sides where unusual problems exist.

In speaking first of the upper group of sinuses I shall say but little of intranasal methods. Intranasal operations are rarely "obliterating" or "eliminating" except as to some of the intranasally placed ethmoids. The drainage that they afford is usually adequate only in cases where the disease changes are mild in character. The anatomical disposition of certain of the ethmoid cells and the sphenoid extensions often makes them inaccessible to intranasal approach. As to the frontal sinus itself, consideration of its anatomical conformation shows why more harm than good has been caused by intranasal manipulation. A review of the literature on osteomyelitis of the frontal bone suggests the contributory inefficiency of intranasal surgery.

The external approach to the fronto-ethmo-sphenoid group of sinuses allows one to satisfy approximately at least the demands laid down by the surgical principles cited. The method that we employ in our service was described by me in 1926. It contributed (1) the employment of local and block anesthesia applied in the orbital depth to the ethmoid and frontal nerve supply, (2) the ligation of

the ethmoid arteries at their orbital entrance into the nose and (3) the ligation of the sphenopalatine artery at or near its nasal entrance, (4) a technic for the removal of the sphenoidal floor, and (5) a provision for permanent drainage of the frontal sinus by use of a flap constructed of nasal mucosa. The value of this last has been much enhanced by adaptations and improvements by my associate, Doctor Robert McNaught.

Prior to the use of block anesthesia and vessel ligation, meticulous work was impossible, particularly on the ethmo-sphenoid group. General anesthesia was universally employed. With the ischemia now afforded one can operate with precision comparable to work in the laboratory on the cadaver. All the cells are investigated before they are opened. Such opportunity makes for efficiency and prevents mishaps. Patients when properly prepared by sedatives undergo the operation with equanimity. They suffer little pain even in revision of former operations, which forms the great bulk of our work.

The incision is small but may be made adequate because ordinarily the scar is not disfiguring. The ethmoid cells are encountered on entering the nose. They form the keystone in the arch of fronto-ethmo-sphenoid surgery. Their obliteration is of paramount importance and can be completely accomplished. Revisions of operations have shown that this important detail has frequently been imperfectly carried out.

In their obliteration the lining mucosa is completely removed. The soft parts of the orbit move in and take the place of the orbital cells. Even some of the intranasal space resulting from removal of the ethmoid mass becomes obliterated by crowding from the orbital soft parts. We sometimes cover the nasal roof of this space by a flap of mucosa dissected from the mesial side of the ethmoid mass.

The operator assumes grave responsibility whenever the frontal sinus is opened. Its complete obliteration cannot be assured without sacrificing its anterior wall. Complete obliteration is rarely advisable. Partial ablation without deformity is attainable. Whatever cavity remains must be adequately and permanently drained. Downward drainage into the nose can be secured only by complete removal of the ethmoid cells. Such technic may be required whenever the frontal sinus is seriously involved. Transethmoidal drainage is maintained by mucous membrane flaps turned upward from the nose. With proper drainage the external wound may be immediately closed even in acute cases. Without proper drainage it gives only a false sense of security to keep the external wound open. Dependence upon

external drainage of a frontal sinus, without elimination and drainage of the ever-present ethmoid disease, is comparable to dependence upon the antiquated Wilde's incision of a mastoid abscess without attention to the mastoid cells. It contributes to establishment of osteomyelitis.

The necessity for elimination of the sphenoid cavity in order to effect a cure was strongly brought out by experiences of my own and others. The usual opening of the thin, anterior wall even without operative disturbance of the mucosa, was disappointing. When injury to, or removal of, the sphenoid lining was added to the operative opening of the anterior wall, a granulating mass resulted so frequently that there was a surgical dictum that the "lining had better be undisturbed."

Finding that the sphenoid recovers no matter how badly involved when the floor is completely removed, led to the development of the following technic. In the course of the fronto-ethmo-sphenoid operation, the sphenoid is opened and studied. If it is obvious that the lining should be removed, the sphenopalatine artery is ligated. A posterior submucous resection allows the removal of the intersphenoid septum. Both sphenoids are thus thrown into one to give sufficient floor space for permanent efficiency of drainage. The entire floor of both sphenoids is then removed. The technic, in my hands, is always difficult to a degree; also there are anatomical anomalies which on rare occasions limit its efficiency. Where it can be properly accomplished the technic is curative. The problem described as occurring in the sphenoid is encountered much more frequently in the antrum. Intranasal methods have their usefulness, but we can hardly expect the cilia to take advantage of an artificial opening, however large, which is not in the direction of their propulsive force; nor can we get effective action from gravity when the opening is not in the most dependent part of the antrum. The Caldwell-Luc technic allows a thorough cleansing of the antrum from diseased tissue, but it offers no more in the way of drainage than the intranasal method. The postoperative drainage is not dependent. Infected material accumulates as before and where the lining has been removed frequently engenders polypoid, scarred and diseased tissue that leaves the patient much worse than he was before. I am surprised at the complacency with which this operation is employed. Through the study of cases at revision, one comes to appreciate the responsibility that is assumed by the surgeon when he removes the lining from the bony walls of any sinus. We know that the sinus mucosa will regenerate, that even the ciliated epithelium is reformed

in a fairly normal fashion. These facts have led to the conclusion that the replacement of a removed diseased lining by a fairly normal, healthy covering is to be expected when the Caldwell-Luc technic is carefully carried out. Such an assumption is wide of the facts.

One classical case furnished conclusive evidence. This patient had been radically operated upon twice by one of our excellent surgeons and also twice by myself with equally unsatisfactory results. A description of this case will make plain the point I wish to emphasize. The patient came under my care some years after two radical operations on each antrum had been done. There was X-ray, gross and microscopical evidence of extensive disease in both antra. Complicating disease made removal of these purulent foci necessary. I was satisfied on finding at operation a polypoid lining and was reassured when I uncovered, under scar tissue, partly walled-off abscesses. There was an excellent opening at the floor of the nose. There could be no fair criticism of the former operator. The patient did not improve. Because of the severe infection and the serious complications, I again repeated the Caldwell-Luc procedure. Again, to make the recital brief—ultimate failure.

I now carried out a procedure that I had been studying in the dissecting room and that seemed to offer a solution to the difficulty. I operated as before and purposely devised a canine alveolar opening, approximately 1 x 2 cm. in size. This opening into the antrum, extending well down on the helpfully edentulous alveolar process, I continued to maintain. Through this large opening I was able to watch the reparative process and learned why the former operations had failed. In the first place, the following morning the antrum was full of clotted blood. With the usual closure of the canine incision it is impossible to prevent this accumulation of blood. It is a painful proceeding to begin transnasal irrigations immediately, and even they would not remove thoroughly such a blood clot. It was difficult to remove even when worked upon directly. Packing the antrum postoperatively does not prevent the accumulation of clotted serum in certain areas; nor does it preclude its accumulations after the packing has been removed.

It was simple to visualize what organization of such clots would lead to. The heavy scarring that so frequently limits the size of the postoperative antrum is undoubtedly due to such an organization. Under ideal circumstances it may be that such organization is of no consequence, that it is even to be desired. Reoperation has convinced me that too frequently substances are included under the clot that later lead to semi-walled-off abscesses. We must acknowledge that,

using the greatest care, it is impossible to be sure that microscopic particles of epithelium are not left to be enclosed by such an organizing clot.

After the sinus had been thoroughly cleaned, another problem of equal importance presented itself. As the bony wall became covered by healthy granulation tissue, this was seen in some places to become redundant. This redundancy was apparently stimulated by small crusts of adherent secretion. These exuberant granulations had to be watched and could easily be conceived as joining others and forming a pocket. At any rate, whatever the theorizing, the fact remained that with the large patulous openings in the most dependent part of the antrums, the cavities became well. It was only necessary to raise the lip at any time to be convinced of the efficacy of the method.

This procedure I have repeated many times. It is always successful when a sufficiently large opening is maintained. It has no affinity with the dental fistulae which have been fought from the time of Highmore. Fistulae rarely cure. While appreciating the disadvantages of this method, I have found it curative in special cases where conditions demand relief.

In conclusion I would say that sinus infection is curable by obliteration or ablation of the cavity. This is not always possible or desirable. It seems, however, that recognition of this fact makes for clear thinking and places the blame for ineffectiveness where it belongs. We become more determined to develop adequate therapy, are more slow to operate, and become more meticulous in applying remedies when we frankly appraise the essential requirements for surgical relief.

STANFORD UNIVERSITY.

XXXIII

HEADACHES OF OTORHINOLOGIC ORIGIN AND CERTAIN REFLEXES CAUSED BY FIFTH NERVE IRRITATION

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DALLAS

In considering the subject of headaches of otorhinologic origin and certain reflexes caused by fifth nerve irritation, it may be advisable to review briefly some of the anatomy of the nose, sinuses and ear with particular reference to the sensory nerve supply to these structures. It is easier to understand why the nose and sinuses give so much trouble if it is remembered that the following anatomic conditions exist in this region. First, the nose is the most prominent portion of the face and is therefore most easily exposed to injury, resulting in deformities of the septum and other abnormalities. It is estimated that 75% of all Caucasian adults have deviated septa, and that in at least 25% of these, the deflection is great enough to cause symptoms.

Second, in the human being there are two of the paranasal sinuses that do not drain by gravity, namely, the maxillary and the sphenoid. This is a distinct disadvantage, for infection in these sinuses is much less likely to subside spontaneously than it would in the frontal sinus where the clearing of infection is favored by gravity drainage. It is probable that for this reason animals that spend much of their time with their noses pointed downward to the ground rarely have a chronic sinus disease, except those that result from dental infection causing trouble in the maxillary sinuses and from trauma to the frontal sinus especially where there has been an injury to horns on cattle, and also to such secondary infection as exists in sinuses that have been blocked by some form of new growth, and in very rare instances of secondary infections that follow severe cases of distemper. Another rather rare condition that occurs especially in dogs is the result of a parasitic infestation of sinuses with the *Pentastoma taenioides* which may produce a very purulent fetid discharge from the sinuses and become a chronic type of trouble.

Third, the nose and its sinuses, from birth until death, are almost constantly subjected to recurrent inflammatory attacks, and these

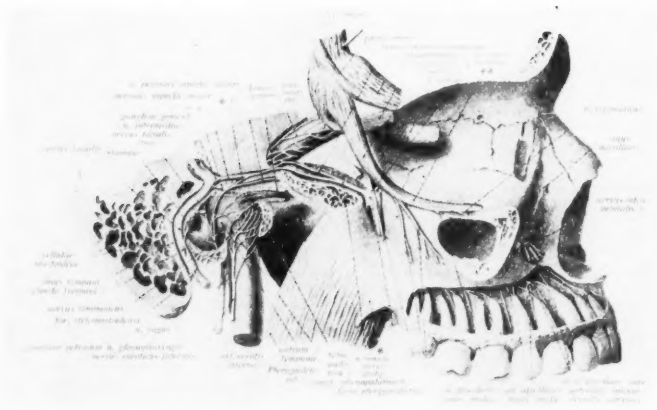

Fig. 1. The second division of the trigeminus, the sphenopalatine ganglion, the intracranial portion of the facial nerve and the tympanic nerve. The great superficial petrosal nerve from the facial nerve and the great deep petrosal nerve from the carotid plexus are shown merging in the pterygoid canal to form the vidian nerve which comes forward to join with a descending branch from the superior maxillary division of the trigeminus to form the sphenopalatine ganglion. (From Sobotta-McMurrich, "Atlas of Human Anatomy.")

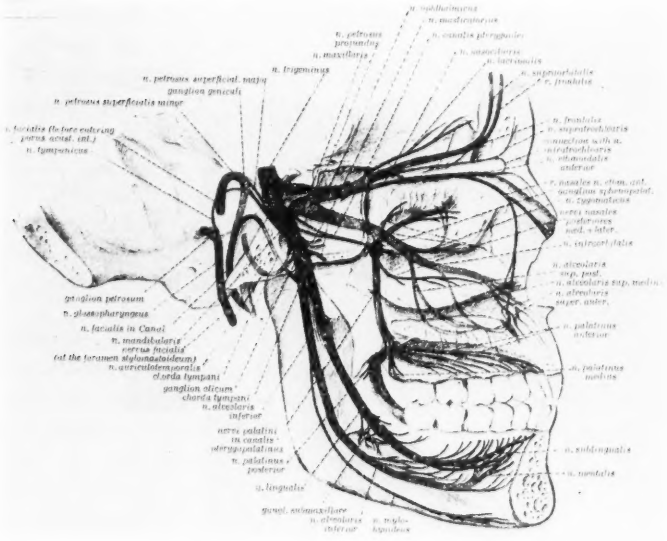

Fig. 2. Branches of the trigeminus and its connections with the facial and glosso-pharyngeal nerve. (Grey nerves are in the bony canals.) (Sobotta-McMurrich, "Atlas of Human Anatomy.")

often leave an indelible imprint on the tissues. These attacks may range from rather mild colds to very severe infections.

Fourth, the center of sensory nerve distribution is the sphenopalatine or Meckel's ganglion. This small bit of nerve tissue is about 5 mm. in length and is located in the pterygopalatine fossa, medial to the maxillary nerve and close to the sphenopalatine foramen. It lies just behind and above the posterior tip of the middle turbinate and just beneath the mucous membrane. Figure 1, from Sobotta-McMurrich, "Atlas of Human Anatomy," shows the second division of the trigeminus, the sphenopalatine ganglion, the intracranial portion of the facial nerve and the tympanic nerve. It can be seen how the ganglion is formed by three roots: (1) the sensory, the sphenopalatinal nerve from the superior maxillary division of the trifacial; (2) the motor, the great superficial petrosal nerve from the facial nerve; and (3) the sympathetic, the great deep petrosal nerve from the internal carotid plexus.

The two latter, the superficial and great deep petrosal nerves, run through the pterygoid canal and become united to form the so-called vidian nerve, which then joins with the sensory branch, the sphenopalatinal nerve, from the superior maxillary. There is really no fusion of the fibers of these various nerves as they form the sphenopalatine ganglion. They remain separate and continue as either sensory, motor, or sympathetic to their terminal endings. The ganglion, however, gives off the following branches: (1) the ascending or orbital branches supplying the mucous membrane of the sphenoidal and posterior ethmoidal cells; (2) the descending or palatine branches supplying the gums, mucoperiosteum of the hard palate, the back portion of the middle and inferior meatal walls, the inferior turbinate, the tonsil, the uvula and soft palate; (3) the internal or nasal branches that supply the septum, the mucous membrane of the anterior portion of the hard palate, the posterior part of the middle and superior turbinals, the posterior ethmoid cells, and the maxillary sinus, and (4) the posterior or pharyngeal branch supplying the upper portion of the pharynx and eustachian tube. Meckel's ganglion is considered a sympathetic ganglion, but since its sensory root is from the fifth nerve, it is directly associated with that important nerve structure, the gasserian ganglion. It is the second largest nerve center outside the cranial cavity, and it innervates and is intimately connected with every region treated by the otolaryngologist. On account of its most extensive distribution it can produce symptoms reflexly to all parts of the head, neck and shoulders. Figure 2, from Sobotta-McMurrich, "Atlas of Human

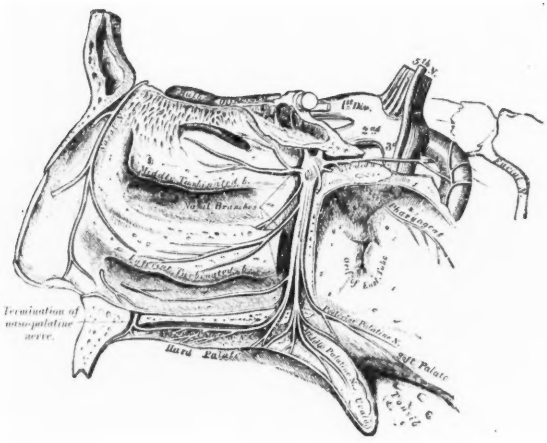

Fig. 3. The sphenopalatine ganglion and its branches. (Gray's Anatomy.)

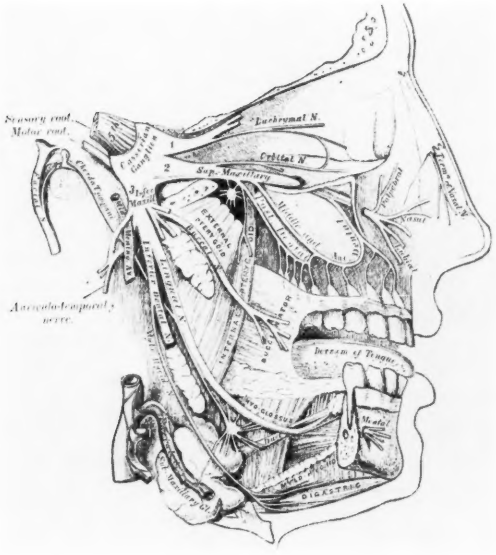

Fig. 4. Distribution of the 2nd and 3rd divisions of the fifth nerve and the submaxillary ganglion. (Gray's Anatomy.)

Fig. 5. Occipital nerves. The suboccipital nerve is the posterior stronger branch of the first cervical nerve. The great occipital nerve is the posterior stronger branch of the second cervical nerve. Together they give motor and sensory supply to the back of the neck and head. (Sobotta-McMurrich, "Atlas of Human Anatomy.")

Anatomy," shows branches of the trigeminus and its connections with the facial and glossopharyngeal nerve. The gray nerves are in the bony canals. Figure 3, from Gray's Anatomy, shows the sphenopalatine ganglion and its branches, while Fig. 4, also from Gray's Anatomy, shows the distribution of the second and third divisions of the fifth nerve and the submaxillary ganglion. In Fig. 4 notice should be given to the superior dental nerves and the infra-orbital nerve, for more consideration will be given to them later. In this illustration these nerves have the terminology of dental nerves, but by many anatomists they are now called the superior anterior alveolar, superior middle alveolar and the superior posterior alveolar nerves. In Fig. 5, another illustration from Sobotta-McMurrich, the occipital nerves can be seen. The suboccipital nerve is the posterior stronger branch of the first cervical nerve. The great occipital nerve is the posterior stronger branch of the second cervical nerve. Together they give motor and sensory supply to the back of the neck and head. Later it will be shown how they synapse on the descend-

ing trigeminal nerve tract and how pain can be referred to the suboccipital area from trouble in the nose.

At this time I shall confine myself to a discussion of head pains directly or indirectly associated with inflammatory conditions of one or more of the accessory nasal sinuses, to pain that results from intranasal pressure, to a few of the more frequent headaches and neuralgias resulting from irritation of the sphenopalatine ganglion, to types of headache encountered in the more common disturbances of the ear, and to certain reflexes caused by fifth nerve irritation.

It is sometimes quite difficult to distinguish between the pain of sinusitis and that due to other causes. It is also true that the pain, or we may term it headache, resulting from disturbed conditions in the sinuses is so variable in its manifestations that it constitutes a most inconsistent and uncertain type of evidence in the domain of symptomatology. During recent years there has been a growing tendency to assume that most of the obscure pains in the head are due to sinus disease, and to overlook the fact that sinusitis can exist without pain. It is true, however, that sinus disease and intranasal pressure are the causes of more headaches than anything else, and we must always consider them as etiologic factors when attempting to diagnose obscure headaches.[28]

The study of nasal headaches resolves itself into a consideration of not only the abnormal conditions in the nasal cavities and paranasal sinuses but also the affections of the adjacent nerve structures.

In sinusitis, the absence of pain proves nothing, but its presence is important and most valuable in making a diagnosis. Neither is the degree of pain a reliable index as to the seriousness of the disease in the sinus. The conditions in and about the nose that give rise to headaches or neuralgias may be classified as follows:[15]

1. Those in which the pain is due to acute inflammation in the nose or paranasal sinuses;

2. Those in which chronic inflammation in these parts is the etiologic factor;

3. Anatomic variations in structure, which result in pressure contact within the nasal cavities; and

4. New growths in the nose and accessory sinuses.

The headache, both as to character, severity, and even time of appearance, depends largely upon the disease present within the sinus and whether such disease is capable of producing some form of pres-

sure. The pressure may result from such a marked swelling of the lining mucosa of a sinus that the membranes of the opposite walls may be in actual contact and the sinus cavity almost, or entirely, occluded. Pressure can also result when the normal openings of sinuses become partially or completely closed, thereby causing stagnation of inflammatory products within the cavities. The pressure of pus would then be exerted against a swollen sensitive mucosa.

Another form of pressure headache which should be mentioned is negative pressure, or so-called vacuum headache. Much has been written about vacuum sinus headache, and there are many otorhinologists who doubt its existence. It is, indeed, difficult to prove by physics that a vacuum can actually exist in a sinus, but the closure of a sinus ostium has been considered by most rhinologists as being sufficient to cause a vacuum in a sinus, and whether a vacuum ever develops or not, certainly there would be a marked swelling of the lining mucosa and probably some fluid transudate thrown into the sinus that could cause enough pull and also possibly sufficient direct pressure on the sensory nerve endings to produce pain. The occurrence of pain in many sinus cases does not appear to be dependent on the presence of pus under pressure but is attributed to the involvement of the sensory nerve endings in the diseased membranes.

The vacuum frontal sinus headache described by Sluder causes intense pain in the frontal sinus, and this headache is aggravated by movement of the eyeballs.

In acute sinusitis there are two types of pain: (1) a constant type that is more or less localized in the region of the sinus, and (2) the neuralgic type, which is periodic.

The pain of acute sinusitis is usually present on arising in the morning or starts shortly thereafter, becoming more severe until early afternoon when it frequently begins to subside. After the headache disappears there may then be a feeling of fullness and pressure in the sinus. The pain is aggravated by stooping or bodily exertion. Each day the pain may be more severe until the peak is reached when there will be a gradual subsidence of symptoms with milder and shorter periods of headache each day. Finally the acute attack usually clears entirely with no more symptoms. In the more severe attacks the pain may be constant, but in such cases the headache is usually worse during the day.

In chronic sinusitis the pain is not so well localized and is rather indefinite. The intensity of the headache bears little relationship to the severity of the infection. There is usually a feeling of dizziness,

heaviness and dullness and an inability to concentrate. Sudden jarring, stooping, severe mental or physical strain, loss of sleep, constipation or dietary indiscretions may intensify the symptoms. Acute colds will greatly aggravate the headaches, which are usually in the same region with each recurring attack.

In acute maxillary sinusitis there may be a dull headache or the pain may be neuralgic. There is usually a sensation of pressure and fullness in the region of the sinus, but the headache will probably be more marked in the frontal region. Some pain may be felt in the upper jaw and teeth. The teeth may feel tender and elongated. The pain is aggravated by stooping, jarring, sneezing, blowing of the nose, and by the excessive use of alcohol and tobacco.

In chronic antral infection there may be no pain, even though there may be severe involvement of the sinus. If the sinus is filled with polyps, cysts or degenerated membrane there may be a sense of fullness but no headache. When headache is present it is usually frontal or infraorbital. If severe pain occurs in these chronic cases it usually indicates marked involvement of the sinus walls. Paroxysms of severe neuralgic pains do occur in some cases and are responsible for the impression that all sinuses are involved.

Headache is the most prominent and constant symptom of acute frontal sinusitis. It is more marked in the early morning, gradually subsiding toward afternoon unless the disease is very severe, when the headache may be constant. The pain is always in the region of the sinus but may radiate to the eye, root of the nose, temple, occiput or vertex. In severe frontal sinusitis the headache may be intense, sickening and throbbing with each heart beat. It may even simulate meningitis.

Chronic frontal sinusitis may or may not cause headache even though marked disease changes have occurred in the lining membrane. Each acute flare-up of a chronic case, however, will likely give types of headaches heretofore described. Neuralgic pains are not common in chronic cases.

The anatomy of the ethmoid sinuses is quite unlike that of the maxillary or frontal sinuses. The ethmoid labyrinth consists of a mass of cells lying within the nasal cavity, whereas the true sinuses lie outside the nasal fossae. This fact accounts for a different type of headache with ethmoiditis than that encountered in diseases of sinuses surrounded by hard unyielding walls.

The ethmoid labyrinths are especially susceptible to two types of disease, namely, the suppurative, which may be acute or chronic, and the chronic hyperplastic type with polyps. In acute ethmoiditis, which is a part of almost every acute cold, there may be some headache during the stage when the membranes are definitely swollen in the region of the midturbinal bodies and the ostia of the ethmoid cells. The pain is felt around the root of the nose, above the inner angle of the eye, about the temples, front teeth, the parietal regions and sometimes the suboccipital areas. It is almost identical in many cases to that seen in acute frontal sinusitis. This headache is due not only to an increased intranasal pressure exerted between highly inflamed membranes, but also to poor ventilation of the ethmoids, antra and frontal sinuses. Of course, under these conditions purulent material may be retained in the ethmoids or other sinuses, and if such material is held under pressure, headache is most likely to occur.

In the chronic types of ethmoiditis, headaches are rather inconstant, the violence of the pain having very little relationship to the severity of the disease. In some cases there may be very little disease associated with most severe headache, and in other instances the disease may be very profound and yet there may be no headache. Generally speaking, the headache encountered in the hyperplastic type is more constant and of a dull aching character, while the headache from the chronic, suppurative type is more often severe but not so constant. Headaches from ethmoiditis are felt particularly in the parietal regions, but if severe, may be in the temples as well. If the anterior cells are especially involved the pain is also likely to be in the brow near the root of the nose, and if the posterior cells are in trouble the pain may be more marked in the occipital region.

Headache from sphenoid disease is probably the most significant of all sinus pains when it is present. It is rather inconstant in many instances. In acute sphenoid sinusitis the headache is an intense sensation of pressure deep in the head, most marked in the posterior half of the head, behind the eyeball, in the vertex and in the mastoid region and middle ear. The pain may be in the supraorbital region. There is frequently a feeling of weight and pressure. The pain may extend downward into the shoulder of the affected side and produce the so-called sphenopalatine syndrome of Sluder. The degree and extent of the pain is dependent upon the amount of pressure exerted within the sinus. The headache is not constant because the degree of pressure is quite variable. The pressure may be due to retained secretion or produced by markedly swollen membranes. If the intra-

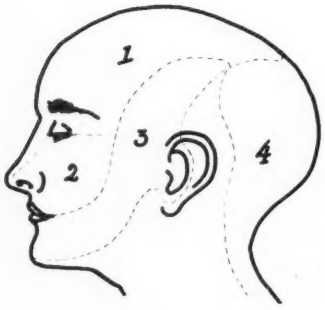

Fig. 6.

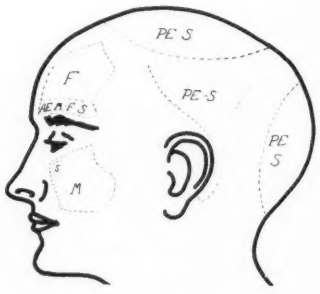

Fig. 7.

Fig. 6. Surface areas of the head supplied by trigeminus and occipital nerves. 1. Distribution of ophthalmic division of trigeminus nerve. 2. Distribution of superior maxillary division of trigeminus nerve. 3. Distribution of inferior maxillary division of trigeminus nerve. 4. Distribution of occipital nerves.

Fig. 7. Areas where pain is ordinarily referred from the various paranasal sinuses. *AE*—Location of anterior ethmoidal headache. *PE*—Location of posterior ethmoidal headache. *M*—Location of maxillary sinus headache. *F*—Location of frontal sinus headache. S—Location of sphenoidal sinus headache.

sinus pressure is very great the headache may be of a throbbing character synchronous with the heart beat. Another rather curious phase of sphenoidal pain is its occasional appearance directly below the eye, in the region of the infra-orbital nerve. Dizziness on stooping is more constantly present with the headache of sphenoidal disease than with any other type of sinusitis.

Figure 6 shows the surface areas supplied by the three divisions of the trigeminal nerve and also the area supplied by the occipital nerves. In the preceding paragraphs an effort has been made to point out the areas where pain is ordinarily referred from the various paranasal sinuses, and in Fig. 7 I have attempted to designate these areas diagramatically.

Intranasal pressure is often the cause of headache. High deviation or thickening of the nasal septum capable of producing tight contact and pressure against the mid-turbinals is frequently the cause of headache of varying intensity. Some patients will develop considerable pain with a moderate amount of intranasal pressure,

whereas other individuals may have considerable amounts of intranasal pressure unassociated with headache. Some people just do not have headaches though the conditions are present in the nose that would ordinarily cause considerable pain. Other people may have rather severe headache from a rather slight disturbance in the nose. The only explanation of this is that the sensitiveness of the sensory nerves is variable to a marked degree. There are many persons who have a moderate degree of intranasal pressure between the septum and the midturbinals and are quite free of pain much of the time, but if for some reason, be it infection, toxicity, exhaustion, dietary indiscretions, or what not, the turbinals should swell moderately and somewhat increase the intranasal pressure, headache will be the result. The pain seems to be increased if the midturbinal is pushed tightly against the side wall of the nose, thereby interfering with proper ventilation and drainage of the ethmoids, frontal sinus and maxillary sinus.

My experience has been that the pain of intranasal pressure is more marked in the early morning. Patients frequently awaken with the headache, and it is associated with some additional blocking of the nose so that at least one nostril is partially or completely closed. If one nostril is closed it is likely to be on the same side on which the patient slept, so that the blocked nostril was the more dependent one. The headache may have awakened the patient or possibly the nasal blocking so disturbed the breathing that the patient was awakened, and then he realized that he had a headache. Many people are susceptible to this type of intranasal blocking and may awaken nearly every morning with headache. A large number of these patients are hypotensive and examination will frequently reveal a low blood pressure and sometimes a minus metabolic rate. Their nasal mucous membranes are very likely to appear pale and boggy with very little tone. There may be a superimposed infection which adds to their difficulties. The person who awakens with this type of headache will usually be relieved as soon as he gets up and moves around. A cup of coffee upon arising does a great deal toward relieving the headache. A warm shower followed by a cold spray across the back of the head and the neck will frequently open the nose within a minute or so. Relief of the headache is obtained as soon as the nose is unblocked and the intranasal pressure is reduced. The headache in these cases is probably due to several things, namely, pressure between the turbinals and the septum with a counterpressure between the turbinals and the side wall of the nose, poor ventilation to the sinuses because the swollen boggy membranes block

the ostia of these cavities, and the retention of secondary inflammatory products within the ethmoids and other sinuses. Surely such patients should have corrected any septal deformity that adds to their difficulties, as they need all the additional space in the nose that they can obtain by rational measures. Frequently these patients should be encouraged to take more exercise in the open air. They really sleep better with their heads elevated on a pillow and with the room well ventilated. If their B.M.R. is low, they should be given their tolerant dose of thyroid.

Otis Wolfe reported a case of severe headache associated with papillitis and marked mental depression. The patient had to be given large doses of opiates for the relief of headache. Examination revealed a very thick septum just anterior to the sphenoid rostrum. It was impossible to pass a probe between the posterior tip of the right midturbinal and the septum. A submucous resection that corrected this deformity was followed by immediate relief of the headache and other symptoms. We have all seen cases similar to this one. Nearly all headaches from intranasal pressure depend upon irritation of the sensory nerve endings in the membrane by some pressure and the effect that such irritation produces on the sphenopalatine ganglion or the anterior ethmoidal nerves.

Intranasal or intrasinus tumors of various types cause headache by the pressure they produce.

Another special type of headache occurs in what F. E. Palmer described in 1926 as the "superior cervical sympathetic ganglion syndrome." There is otalgia and unilateral headache together with a tender area in the side of the neck over the location of the superior sympathetic ganglion, associated with a nasopharyngitis. No complaint is made of the tender area, but it can be easily found on examination. Pressure on the area increases the headache and otalgia, which decrease when the pressure is released. Examination of the ears is negative and that of the sinuses is likely to be so. Cocainization of the sphenopalatine ganglion may or may not give relief to the otalgia. The whole syndrome clears up when the nasopharyngitis gets well.

If any branch of the trifacial nerve is irritated by trauma, pressure or an inflammatory process there may be referred pain to any part of the head, eyes, face, teeth, lower jaw, neck, throat, suboccipital region, shoulder girdle and down the arm to the fingers. A number of reflexes such as writer's cramp, dilated pupil and hiccough can be the result of irritation along some branch of the tri-

geminus, and I shall attempt to explain some of these reflexes by illustrations showing how the nerve arcs are completed. Of course, these phenomena can be caused by other things than trigeminal irritation, but the fact remains that irritation of the trigeminus is the direct etiologic factor in their production in some cases.

I should like to call your attention to a syndrome that I have observed on several occasions. A disease of the anterior ethmoidal cells or pressure exerted by a deviated septum against the anterior half of the middle turbinal body may cause pain in the front three or five teeth of the upper jaw. I have often relieved aching of the teeth by cocainizing the region of the anterior half of the middle turbinal and anterior ethmoidal area. Some dentists have told me that aching of these teeth has been responsible in some instances for extraction, and no disease was found at the roots of the teeth. The aching was not relieved until some intranasal work was done. If the pain has been quite severe for several days and the inflammatory trouble in the nose gradually subsides or becomes quiescent, the aching in the teeth may change to a feeling of numbness for several days as if the teeth were devitalized. It acts to some extent as if a true neuritis had been produced. In order to explain this syndrome the path by which the pain is referred should be traced. I suugest that you now refer to Fig. 8, which is a diagram showing how pressure or inflammatory reaction on the terminal twigs of the anterior ethmoidal nerves can set up a stimulus that will be interpreted as pain in the teeth. The pain stimulus would originate in the terminal twigs of the anterior ethmoidal nerve as they are distributed over the anterior half of the midturbinal body and the anterior ethmoidal cells. The anterior ethmoidal nerve comes off from the nasociliary nerve, which is a branch of the ophthalmic nerve or first division of the trigeminal. The peripheral process of the primary neuron extends to a supporting cell in the gasserian ganglion, and from this supporting cell the central process of the primary neuron extends to the posterior surface of the pons. The anterior and middle superior alveolar nerves come off from the infraorbital nerve in the infraorbital canal and give nerve supply to the front five teeth. The infraorbital nerve is the main continuation forward of the superior maxillary division of the trigeminus nerve. The peripheral process of this primary neuron therefore extends from the front teeth to a supporting cell in the gasserian ganglion, and the central process of the primary neuron extends from the gasserian ganglion to the pons. In the posterior portion of the pons are the nuclei of the second neurons on which the respective primary neurons, just described, synapse. Both of the primary neurons synapse in the pons around the nuclei of the

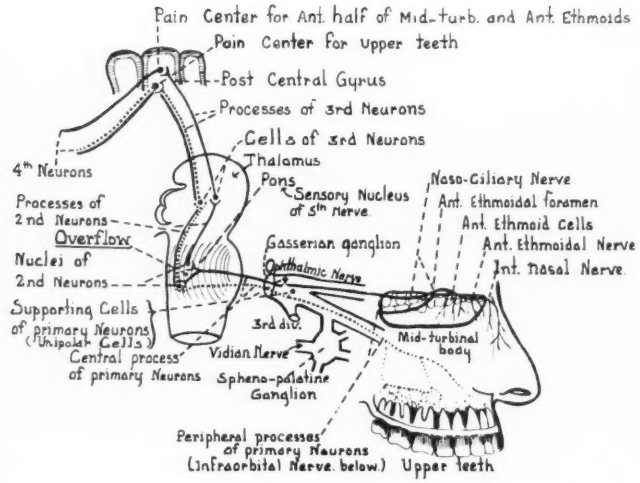

Fig. 8. Diagram of pain referred from nose to teeth.[14]

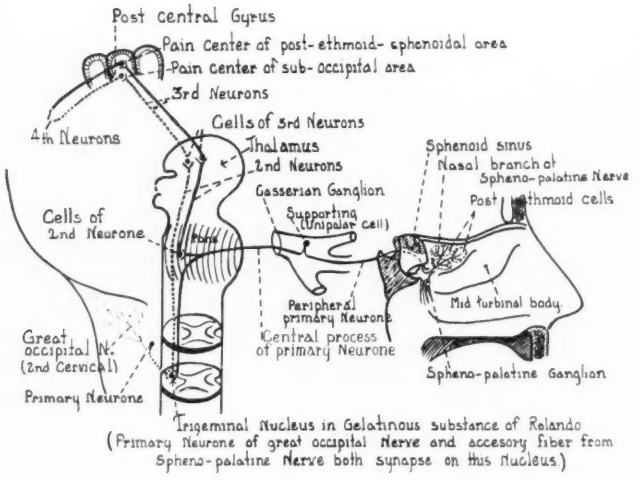

Fig. 9. Diagram of pain referred from nose to suboccipital area.[14]

second neurons. These nuclei are in close proximity, and there may easily be an overflow of stimuli from the central process of the primary neuron coming from the midturbinal body to the nucleus of the second neuron onto which the primary neuron from the teeth synapses. The second neuron from the teeth would then be carrying the stimulus that originated in the anterior half of the midturbinal body and anterior ethmoids. The second neuron then synapses in the thalamus with the nucleus of the third neuron, which carries the pain stimulus to the pain center in the post-central gyrus of the brain, where the stimulus is interpreted as pain in the teeth. The third neuron probably synapses in the post-central gyrus with a fourth neuron that carries the stimulus to other cortical areas. This is really a false interpretation on the part of the brain as to where the stimulus for the pain actually originated, but to all intents and purposes the pain is actually in the teeth as if the stimulus for it originated there. The trouble is actually in the nose, and the pain is in the teeth.

Pain at the base of the skull that we may call suboccipital headache, indurative occipital headache, nodular trapezius headache or rheumatoid headache of the occipital region, can be explained definitely by irritation along the sensory branches of the sphenopalatine ganglion, the ophthalmic division of the trifacial, the alveolar nerves coming off of the infraorbital, or the terminal branches of the mandibular nerve. This would be a direct referred pain, and the neurons with their synapses can be anatomically traced back to the pain center of the trigeminus in the post central gyrus and possibly to other areas in the cortex of the brain. Figure 9 shows how this type of suboccipital headache can result from some type of irritation produced on the sphenopalatine nerve. If we assume that the source of irritation is in the inferior turbinal body the stimulus would be carried back through the sphenopalatine nerve, which is the branch of the superior maxillary nerve that comes down through the sphenopalatine ganglion. The impulse would travel through the S.P.G. and the gasserian ganglion to the pons, where the primary neuron would synapse with the nucleus of the second neuron, thence to the thalamus, where the second neuron would synapse with the nucleus of the third neuron, thence to the pain center in the post-central gyrus, where the third neuron may synapse with the nucleus of a fourth neuron that would connect with some other cortical area.

In the pons the primary neuron from the inferior turbinal body splits and sends a fiber down the trigeminal tract in the cord as low as the fourth cervical vertebra. This tract is located at the apex of

the posterior horn, and neurons in this tract synapse with trigeminal nuclei in the gelatinous substance of Rolando. The primary neuron from the inferior turbinal and the primary neuron of the great occipital nerve may synapse on the same nucleus of the trigeminal nerve in the gelatinous substance. In this instance the pain stimulus in the inferior turbinal would be carried to the pain center of the suboccipital region in the post-central gyrus and result in pain in the suboccipital region from a stimulus in the inferior turbinal region. In cases of eye strain there is frequently an aching in the suboccipital region, and the mechanism of the referred pain is exactly the same except that the source of irritation is in the eye, and neurons in the ophthalmic division of the trigeminus would carry the impulse back through the gasserian ganglion to the pons.

We are all familiar with Sluder's "lower half headache," in which the pain may begin at the root of the nose, in and about the eye, the upper jaw and teeth, sometimes also the lower jaw and teeth, and extends backward to the temple and about the zygoma to the ear, causing earache emphasized at the mastoid but always severest at a point about 5 cm. back of that, and reaches back of that area by way of the occiput and neck causing pain in the shoulder blade and shoulder and less often in the axilla and breast. In more severe attacks the pain may extend into the arms, forearms, hand and finger tips. Sluder believed that most cases of sore or stiff neck attributed to myalgia, neuralgia or sternomastoid rheumatism, are in reality sphenopalatine neuralgia.

He also cited cases in which cocainization of the sphenopalatine ganglion relieved burning tongue, peritonsillar abscess, otalgia, eye pain, pain of tuberculous laryngitis, itching of the outer ear canal, hiccough, asthma, writer's cramp and upper jaw toothache. Sluder's clinical observations were quite correct, but his anatomical explanations of how the reflexes occurred were not always clear. As a matter of fact, he did not explain the anatomy of some of these reflexes, though I'm sure he had worked them out to his own satisfaction. By diagrams I shall endeavor to clarify some of these symptoms because it is not only valuable to know that a certain symptom can occur from irritation of some branch of the trigeminal nerve, but it is also very worthwhile to understand that the symptom can be explained anatomically. I believe that completed nerve arcs can be traced that will account for all the symptoms that Sluder has enumerated and that probably there are several other symptoms that he did not mention that can be explained by the same process.

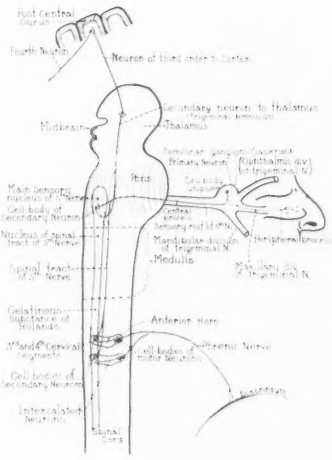

Fig. 10.

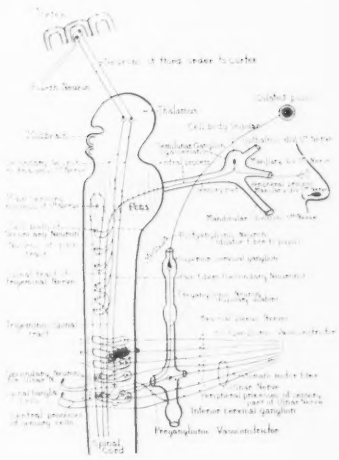

Fig. 11.

Fig. 10. Hiccough reflex resulting from stimulation of maxillary division of the trigeminal.[14]

Fig. 11. Writer's cramp and pupillary reflexes with pain in hand resulting from stimulation of maxillary division of trigeminal nerve.[14]

Figure 10 shows how hiccough can be a reflex contraction of the diaphragm produced by an afferent stimulus on some branch of the fifth nerve, in this instance, the superior maxillary. This afferent stimulus is conducted by the primary fibers of the fifth nerve to the nuclei of the fifth nerve in the pons and the gelatinous substance of Rolando in the upper segments of the spinal cord. The secondary neurons, or intercolated neurons, are in the posterior horn and send their fibers to synapse on the anterior horn cells in the third and fourth cervical segments, which in turn give rise to the phrenic nerve. The phrenic nerve conducts the motor impulse to the diaphragm, causing the contraction of that organ. Hiccough is therefore purely a sensory motor reflex in this instance.

In Figure 11 I have attempted to show how irritation along the maxillary division of the trigeminal nerve can cause a dilatation of the pupil, writer's cramp, and pain referred to the arm, hand and fingers. Sluder stated that the latter two symptoms occurred but he said nothing about dilatation of the pupil, which I believe can result from a stimulus along some branch of the trigeminal. Dilatation

of the pupil and writer's cramp can be explained as follows: In the diagram the afferent impulse originates in the peripheral process of the superior maxillary division of the trigeminal, which carries it through the semilunar ganglion and into the pons, and down the pons and medulla, synapsing upon the cells of the nuclei of the spinal tract of the trigeminal nerve. Cells of the nucleus of the spinal tract of the fifth nerve send fibers down the cord and constitute the trigemino-spinal tract. The trigemino-spinal fibers synapse upon the various anterior horn cells throughout the greater portion of the spinal cord. They also synapse upon the preganglionic neurons comprising the thoracico-lumbar autonomics. The preganglionic fibers of the first thoracic segment enter the ganglionated trunk through the white *rami communicantes*. Those that produce dilatation of the pupil ascend in the trunk to the superior cervical sympathetic ganglion where they synapse upon the postganglionic cells. These postganglionic cells send fibers by way of the internal carotid and cavernous plexus into the eye, where they supply the dilator or radial fibers of the pupil. This produces a dilatation of the pupil. Other preganglionic neurons in the upper thoracic segments send fibers through the white rami of the respective spinal nerves to the ganglionated trunk where they synapse upon the postganglionic neurons. Those that supply the blood vessels of the upper extremity synapse upon the postganglionic cells in the middle and inferior cervical ganglia. These postganglionic cells send their fibers by gray *rami communicantes* of the nerves comprising the brachial plexus. Thus we have a reflex arc which is capable of producing a constriction of the blood vessels of the entire upper extremity with resulting anoxemia in the distribution of the nerves in the upper extremity. The anoxemia produces an irritation of the sensory nerves, and also causes the cramping. The irritation of the anoxemia sets up pain impulses in the distribution of the sensory nerves of the brachial plexus, and these pain impulses travel into the cord by way of the nerves supplying the upper extremity. The primary neurons of those nerves synapse upon the gelatinous substance in the posterior horn of the corresponding spinal segments. These secondary neurons send their fibers by way of the pain or lateral-spino-thalamic tract to the thalamus, where they synapse upon the third neuron that carries the impulse to the post-central gyrus of the cortex.

It is possible that some of the upper extremity pain, especially that of the ulnar, is of the referred type. This symptom can be explained as follows. As already stated the afferent impulse enters the pons through the trigeminal nerve fibers or primary neurons. It is

said that many of the processes of these neurons descend a considerable distance into the spinal cord. In the cord it is believed that many of these synapse upon the cells comprising the secondary neurons, receiving impulses from the primary pain neurons supplying the upper extremity. We therefore have a false impression in the form of pain in the upper extremity, possibly all the way to the finger tips, when as a matter of fact it is the result of a stimulus originating in some branch of the trigeminal nerve.

Reflex asthma from trigeminal nerve irritation can and undoubtedly does occur. The reflex arc explaining it is more easily traced than in the instance of writer's cramp or of dilatation of the pupil. On account of the length of this paper all of these symptoms cannot be explained in detail.

I wish to call attention to the fact that earache can be caused by otitis media, mastoiditis, faulty dental occlusion and eustachian tube blockage. In otitis media and mastoiditis of moderate severity, the pain is principally in the ear and the mastoid region, but in severe cases the pain may be referred to the temples, parietal and occipital regions, and into the lower jaw. It may become a rather severe type of dull throbbing headache in the regions mentioned.

Mandibular joint defects and malocclusion are disturbances that are frequently overlooked as causes of pain in the ear. The patient may easily attribute the earache to disease of the ear itself or as referred pain from a sinus. Malocclusion and overbite may not be suspected as causes for the earache and headache, because there are so many other medical, rhinologic and ophthalmologic reasons for headache distributed about the ears, vertex and occiput. In these cases there may be some type of sinus disease actually existing and the sinus trouble may receive all the attention by the physician, and yet measures directed to clearing the sinus disease will be ineffective in relieving the earache. According to James Costen, "The diagnosis of this condition is established by: 1) the lack of molar teeth or badly fitting dental plates permitting overbite; 2) mild catarrhal deafness improved at once by inflation of eustachian tubes; 3) dizzy spells relieved by inflation of tubes; 4) tenderness to palpation of mandibular joints; 5) marked comfort to patient from interposing a flat object between the jaws; 6) the presence of the typical headache after sinus or eye involvement has been corrected; also the presence of typical headache when sinuses or eyes are found to be negative." The headache is severe and rather constantly localized to the vertex and occiput and behind the ears. It increases toward the end

of the day, which is not true of typical sinus headache but more suggestive of eye strain. There is frequently a burning sensation in the throat, tongue and side of the nose. The relief of symptoms in these cases will depend upon: 1) the accuracy with which dentures can be made to relieve the abnormal pressure in the temporo-mandibular joint and 2) the extent of injury to the eustachian tubes and to the condyle, the meniscus and the joint capsule. It is quite possible that mandibular joint damage may be the cause of glosso-pharyngeal neuralgia, the association of the chordi tympani and auriculotemporal nerves with the ninth occurring via sensory connections to the otic ganglion.

The frequently recurring headaches of hyperplastic post-ethmoid sphenoiditis may be easily mistaken for migraine. In migraine there are no demonstrable local lesions which might cause the headache; therefore, the headache of sinus disease cannot be classed as migraine. It is probable that migraine is an allergic phenomenon, and surely a hereditary influence can be traced in nearly all cases. Among the relief measures for migraine we must consider the removal of infected tonsils and the cleaning up of sinus disease because of the possibility of focal infection generating a toxin that may precipitate the allergic reaction that causes the migraine. It is also probable that there is an endocrine imbalance that serves as an etiologic factor in causing the headache in some migraine cases. The tonsils and sinus infection may have an influence in upsetting the endocrine balance—thus another reason for clearing these patients of all focal infection, if possible.

It is not intended to discuss extensively the measures for relief of the various types of headache mentioned. However, in order to give any permanent type of relief in these cases, it is necessary to clear up either by surgery or treatment, any sinus disease that exists, relieve intranasal pressure by correcting deviated and thickened septa, establish good ventilation and drainage to the sinuses and remote portions of the nasal chamber. Cocainization and alcohol injections of the sphenopalatine ganglion are most valuable at times. Of course, any case of otitis media and mastoiditis should be handled by surgery if necessary, but the disease must at least be controlled in some way.

SUMMARY AND CONCLUSIONS

1. Sinus disease, faulty ventilation to the sinuses and intranasal pressure account for the greater number of headaches.

2. Regardless of whether a vacuum is formed in a closed paranasal sinus, headache is likely to occur where the natural ostium is blocked.

3. A moderate amount of intranasal pressure may exist without symptoms, but if increased by swelling of the nasal membranes from some type of toxicity, with a secondary effect of poor ventilation and drainage to the sinuses, headache will probably result. This is especially true if the midturbinal swells to the extent that it is pushed tightly against the side wall of the nose.

4. Acute sinus disease is nearly always associated with pain, whereas chronic sinusitis may exist without any history of headaches.

5. Some people may experience very little pain though considerable sinusitis and intranasal pressure may exist, whereas other people may suffer severely from a very small amount of intranasal pressure and a negligible amount of sinusitis.

6. The pain of disease in a certain sinus is usually referred to certain areas of the skull, and a thorough knowledge of these facts is very helpful and sometimes almost essential in making an accurate diagnosis. The history by the patient may be far more valuable in some instances than would be the physical examination, transillumination and X-ray study.

7. Sluder's clinical observations regarding lower-half headache and certain symptoms resulting from irritation of the sphenopalatine nerve were eminently correct, and it is probable that all of these symptoms and others can be satisfactorily explained by tracing the reflex arcs anatomically.

8. Mandibular joint defects and malocclusion are rather frequently the cause of pain in the ear which may appear to be referred from a sinus. Careful study of the case should simplify this diagnosis.

9. Migraine is frequently mistaken for pain of sinusitis or intranasal pressure, but migraine is probably an allergic phenomenon in which there is hereditary influence. In migraine there are no nasal or sinus lesions demonstrable to explain the headache. It is of especial interest to the otolaryngologist, because in migraine cases it is very essential to remove any focal infection that may be responsible for an allergic reaction or capable of causing disturbances in the endocrine mechanism.

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XXXIV

SOME OBSERVATIONS ON NASAL NEUROLOGY*

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Diagnosis and therapy in the nose and accessory sinuses have run the gamut from empiricism to surgical radicalism, and now back again to the intricacies of biochemistry and cellular physiology. One of the most confusing divisions of nasal anatomy has resisted accurate exploration for a long time, and only recently some of its mysteries have been cleared up. Nevertheless, the innervation of the nose remains one of the most important factors in any study of this region. This importance is ordinarily brought to our attention because of the production and transmission of pain—discomfort, sensitiveness—as an evidence of disturbed or interrupted function.

Protective reaction to unfavorable environment, which may reach sufficient intensity to cause pain in higher forms of life, is responsible for all sorts of defensive mechanisms; it has led in lower forms to the creation of specialized perceptive cells, which have through evolutionary processes built up connecting fibers, sensory tracts, central organs of discrimination, motor tracts and specialized endings. Along with these higher functions, the lower vegetative neural apparatus has learned to carry on "without thinking" all the multifarious necessities of the circulation, of digestion, of excretion, of heat control and all the rest.

Leave out of account the olfactory apparatus, which like the retina is essentially a tract continuing directly forward from the brain. The true sensation nerves of the nose and sinuses have been crowded together by the development of binocular single vision through anterior direction of the orbits and by consequent reduction in size of the nasal cavities and increase in tortuousness of nerve canals and foramina. Hence they are rather easily disturbed when things go wrong anywhere in their somewhat complicated neighborhood. One of the most important parts of our training as otolaryngologists relates to the location of these nerves and the various referred pains for which they may become responsible.

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We are, however, prone to forget the role of the autonomic system, which does not react to actual traumatic skin or mucosal or osseous pain-sensations; here we find the sympathetic and parasympathetic control of the input of blood, and outflow of mucus and serum. Pain, felt along the other system, may be caused by swelling or ischemia. Here come in responses to allergens, pathogens, gases; reactions to wrong proportions of oxygen and carbon dioxid or to wrong proportions of water vapor—excessive or deficient humidity, "air conditioning", and the like. Entrance of water to the nasal chambers is rather a traumatic than an actual autonomic irritant; but autonomic reflexes reach the nose rapidly from the rest of the body surface or from the esophagus and the stomach, that is from chilling of the body or the extremities, or from the ingestion of very hot, cold or highly flavored foods. Sneezing and nasal dripping, hypersecretion thus originated, and redness of the external nose later showing up as permanent dilation of capillaries, evidence the potency of these autonomic factors. The input of certain cells—eosinophils in allergic persons for example—may not be altogether chemotactic; at any rate autonomic influence assists with the necessary added flow of blood to the engorged turbinates in such individuals.

The otolaryngologist has reason occasionally to note the vasomotor effects of fear before the use of any instrument or drug. Syncope, with dilated pupils and occasional epileptiform movements, will also be found to show pale nasopharyngeal mucosa and wide open passages. Severe shock, pain elsewhere in the body, even sudden fright, will leave the turbinates relatively bloodless; the inward parts become ischemic as the face gets pale. In susceptible people this fright-ischemia may be accompanied by severe throbbing lumbar pain, the so-called "adrenal crisis". Contrast with these appearances the congestion and turgidity of anger, of excitement, of heavy eating or drinking. Cases of extreme nasal stuffiness due to sexual stimulation are not infrequently reported by gynecologists, urologists, and psychoanalysts. The role of emotion in the vasomotor control of the nose may thus be very considerable.

Let it be admitted that so far we have little or no control of these autonomic systems, and that a vicious cycle of unpleasant vasomotor effects may be very hard to arrest. The so-called "histamin headaches", with which neurologists and neurosurgeons have been experimenting lately, bear a certain resemblance to the old-fashioned "nasal congestive headaches" which were ascribed to chronic constipation. May it not be possible that vasomotor (pain) effects in the

dural circulation may occasionally have their origin in histamin concentrations in a filthy antrum wall, as well as in the highly resistant intestinal mucosa?

At any rate, we know that headache and pain from the nose may usually be relieved if we can find and block the appropriate pathway. This is of course not always possible; and such well-blazed pain pathways may be shared by irritation from muscular imbalance or from refractive error, especially hyperopic or mixed astigmatism.

Pain should never be the sole indication for an operative procedure. It is a leading diagnostic symptom, truly, but every other avenue of diagnosis should be followed before operation is undertaken. One sees occasionally some unhappy individual who has every sinus standing wide open to the winter wind, with his pain far worse from scar tissue than it was to begin with. Such people become hypersensitive to cold and dryness, and would gladly revert to the old wet drippy nose if it were possible. Of course such situations must not weigh against the lifesaving value of many radical procedures. They give point to the axiom that operations within the nose should, so far as possible, restore physiologic function and proper sinus drainage, without too much interference with normal nerve pathways, whether autonomic or sensory.

Since the days when Sluder[1] was making his monumental compilation on referred pain, it has become a commonplace that reflex discomfort may work upward, downward, in or out, depending upon the structures involved and their vasomotor as well as their sensory nerve connections. Reference of pain from antrum to forehead, from larynx to cheek or eye, he was able to interrupt by destruction of the "junction box", the sphenopalatine sympathetic ganglion through which also pass so many sensory fibers to nose and eye and back into the temporal bone. It has however been definitely established that many sympathetic and parasympathetic connections (as for example in the carotid plexus) cannot all be destroyed by operation; that some fibers persist, and that others grow back within a few months, restoring circulatory balance, and, unhappily, the discomforts for which the difficult nerve excision was originally made.

Reverting to the problem of referred pain pathways from the nose, it may be recalled that Ramsay Hunt mapped the sensory area of the seventh nerve behind and within the concha more than thirty years ago, in connection with his study of herpes zoster oticus.[2] Larsell was able to demonstrate the autonomic and microscopic connections of this nerve in the Casselberry Prize essay for 1928.[3]

The sphenopalatine ganglion is connected not only with the maxillary division of the fifth nerve, but has a large posterior branch, the vidian nerve, which divides into the great deep, and the great superficial petrosal nerves. The latter contains large myelinated fibers of sensory type, which connect in the geniculate ganglion with the sensory distribution of the facial nerve.

This distribution corresponds exactly with the areas involved in herpes zoster oticus, namely the posterior surface of the concha of the ear, the skin over the mastoid, and a variable area within the concha and along the posterior wall of the external auditory canal.[2] A direct sensory nerve connection is thus seen to exist between the sphenopalatine region of the nose and the skin of the ear. Clinical discrimination between these sharp pains and actual ear or mastoid involvement offers little difficulty, since cocainization of the ganglion area ordinarily arrests this symptom.

No such direct pathway exists, however, for referred pain to the trapezius muscle and the occipital and deltoid regions. Further studies were therefore directed toward the vasomotor innervation of the nose.[4]

Just as pain may occur in an extremity owing to interference with its vascular supply, being referred to the appropriate spinal segment even though the disturbance arises through the autonomic system, it was reasoned that similar vascular difficulties in the very complex head and neck region might be projected into the sensory domain of some cervical nerves.

Vasodilator and secretory fibers reach the nasal mucosa from the vidan nerve through the sphenopalatine ganglion. Vasoconstrictor impulses seem to travel upward from the superior cervical sympathetic ganglion to and through the sphenopalatine ganglion while vasodilatation and secretion seem largely to be controlled by fibers which form a part of the great superficial petrosal nerve.[5]

Experimental evidence based on local anesthesia and ischemia of the mastoid skin in persons suffering from referred pain from the sphenopalatine region—anesthesia blocking such referred pain and ischemia producing it—suggested further examination of the circulation of the rabbit's ear.

It was found, after section of the maxillary nerve, thus excluding the fifth, that faradic stimulation of the sphenopalatine region produced marked vasoconstriction in the ear.[6] These impulses must

have traveled by the posterior nasal, great superficial petrosal, and possibly the deep petrosal nerve. Vasoconstriction was found to be abolished, however, by section of the cervical part of the spinal cord at the level of the sixth spinal segment, or by section of the cervical sympathetic trunk between the middle and inferior cervical sympathetic ganglia.

Since these regions of the neck and shoulder are affected by reflex ischemia actuated by stimulation of the sphenopalatine area of the nose, pain is referred to the ischemic areas, as elsewhere in the body. The nervous pathways involved are therefore the nasal and palatine branches of the sphenopalatine ganglion, the great superficial petrosal nerve, the connections within the medulla oblongata with the reticulospinal tract (the reticulospinal path arises from generalized cells in the medulla oblongata having to do with the conduction of vasomotor and other sympathetic stimuli) and, through those, the connections with the segmental autonomic nerves in the lower cervical segments of the cord. Impulses passing along the reticulospinal tract make connections with the preganglionic fibers of the sympathetic vasoconstrictors which arise from the lower part of the cervical and the upper part of the thoracic portion of the spinal cord, thus affecting the arteries of the ear and adjacent structures.

It is therefore unnecessary to ascribe to the cervical sympathetic any rôle in pain transmission save its well-established function of vasomotor and secretory regulation. But when, in the nose, interference with normal autonomic regulation occurs, the altered situation may be referred to distant regions in the ear, neck and shoulder through the cervical sympathetic and its anterior-root connections with the spinal cord and up to the brain.

It seems reasonable to assume that ischemia in a muscle may lead to pain; conversely, a painful muscle, even if the pain "felt" therein be referred, will be held as nearly motionless as possible, thus prolonging either local ischemia or local anoxia or both. Herein may perhaps lie the true explanation of cervical myalgias, indurative headaches and similar phenomena which have so far challenged accurate analysis. It would certainly seem wise to attempt diagnosis of such symptomatic manifestations by local and intranasal anesthesia before subjecting them either to cervical root section by the neural surgeon or allowing them to fall by default into the hands of unqualified masseurs masquerading as adjusters of alleged vertebral displacements.

The physiology of the nervous system (most complex, since it is the master key to all) is at last undergoing electrical and physiochemical tests which are opening unexpected vistas toward future diagnostic and therapeutic procedures. Apparently of utmost importance in our field is the matter of autonomic control. Sensory nerves—the fifth, whether nasociliary, sphenopalatine or palatopharyngeal, or the sensory seventh, or minute branches from these to the dura of the anterior and middle fossae—react at the mercy of those ancient involuntary, vegetative mechanisms which carry on our functional life, asleep or awake.

Control of these autonomic endocrine nerve systems will eventually be managed so as to build resistance to viruses and pathogens entering the upper respiratory gateway. Similarly, proper utilization of vitamins and appropriate distribution of hormones will probably be effected, while the toxic inhibitions arising from powerful aminocompounds and other harmful protein molecules will be adequately controlled.

One must acknowledge with gratitude the pioneer work of such master neurologists as Herrick, Ranson and Larsell. Their anatomic discoveries must not be related to the electronic measurements of active currents and to the biochemic results of such currents as affecting the blood, all its circulating components, and the endocrine glands. For such further studies the average clinical otolaryngologist must depend upon the achievements of research laboratories. Nevertheless, it is upon the observation of many careful clinicians, and upon their intelligent questioning, that the research scientist must depend for eventual demonstration of the practical value of his theories. Neither group can progress satisfactorily without the other. In such voluntary collaboration, thus far unimpeded in this free land, lies the hope of our people for health in the future.

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XXXV

TREATMENT OF ACUTE INFECTIONS OF THE FRONTAL SINUS*

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The majority of upper respiratory infections are due to the common cold virus, but pyogenic organisms play the chief role in the complications, i.e., sinus infections. The mucous membrane lining the nasal cavities and accessory nasal sinuses forms a continuous sheet, which is rich in blood vessels and mucus-secreting glands and is covered with ciliated epithelium. An acute infection is the result of impaired function of ciliated epithelium and mechanical occlusion of the orifice of the sinus by edema and thick discharge. The severity of the clinical symptoms depends on the degree of obstruction to drainage and the virulence of the organism. If recognized during the acute stage, all sinus infections can be cured by simple local treatment or operative measures which re-establish drainage; if allowed to become chronic, however, the infection is often extremely difficult or impossible to cure. We wish to emphasize in this paper the fact that early recognition and establishment of adequate drainage in acute sinusitis is the only way to prevent the development of chronic sinusitis and its sequellae.

Many patients with acute sinusitis recover spontaneously or after such simple measures as: a few days rest in bed, a mild laxative, forced fluids, the local application of heat (hot compresses, diathermy or the infra-red lamp) and the use of a non-irritating astringent, such as ¼% aqueous solution of neosynephrin used as nasal drops with the patient in the Proetz position. A word of warning should be given here regarding chemotherapy in acute infections of the accessory nasal sinuses. The conditions in sinus infection are identical with those in acute suppuration in the mastoid. In both the pus must have a free outlet for drainage, either externally or through the

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natural pathways to the nasal cavity or pharynx. The pain, fever and leucocytosis of an acute mastoid infection (the symptoms we depend on most for an indication of the progress of the disease) promptly disappear after chemotherapy and we are lulled into a feeling that all is going well, only to have evidence of a deep-seated infection and bone necrosis appear two or three weeks later and the need for operation become urgent. The danger of meningeal infection and abscess from a masked frontal sinus infection is just as great as it is in a mastoid infection. For this reason it is safer to establish drainage before giving sulfanilamide or similar drugs.

If the pain and local tenderness over the frontal sinus are severe after 24 hours of conservative treatment, we prefer to make a small external opening for drainage rather than to remove the anterior end of the middle turbinate, open the ethmoidal cells or employ any other form of intranasal surgery. The chief objection to intranasal operation in acute frontal sinus infection is the danger of traumatizing the mucous membrane lining the nasofrontal duct, and thus converting an acute sinusitis, due to temporary occlusion of the duct by edematous mucous membrane, into a chronic condition, due to permanent stricture of the nasofrontal duct with granulations and polyps. Acute sinusitis is primarly an infection of the mucous membrane and not of the bone, and as a rule free drainage is all that is necessary to cure it. Chronic sinusitis is difficult to cure by any simple measure. Therefore it is of the greatest importance that the acute infection be treated in such a way as to prevent the transition to the chronic state.

During the past five years we have treated 36 patients with acute frontal sinus infection by the following method. A skin incision (¾ of an inch in length) is made in the hair line of the eyebrow, just above the inner canthus of the eye. On account of the extreme sensitiveness of the periosteum we use a combination of avertin, nitrous oxide and oxygen rather than local anesthesia. It is important that the skin and subcutaneous tissues be handled with the greatest gentleness when retractors are used and the periosteum elevated. It is also important to avoid cutting the supraorbital nerve and vessels. Bleeding points are picked up with the finest (mosquito) artery clamps and ligated by transfixing the tissues on each side of the clamp with a small needle carrying No. 00 plain catgut. The periosteum is elevated just enough to allow an opening (½ inch in diameter) to be made in the bone with a perforator and burr.

The success of this frontal sinus operation and the absence of complications depends on the selection of early acute cases and the

technique of the operator. The important part of the technique is the avoidance of injury to the skin, periosteum, bone and mucous membrane lining the frontal sinus. When exposed with the burr the mucous membrane of the sinus often protrudes into the wound, due to pressure of secretions and gas in the sinus. A culture is made as a guide for subsequent chemotherapy. A fibrinous plug of mucopurulent material is usually found in the sinus, and no doubt is responsible in part for the occlusion of the nasofrontal duct. It is best removed with suction, using a small eustachian catheter as a suction tube. The mucous membrane lining the sinus is hyperemic, edematous and sometimes polypoid. The greatest care must be taken to avoid injuring this mucous membrane. After removing the secretions with suction the interior of the sinus is irrigated with hot physiological sodium chloride solution, but it should not be touched with a curette, or wiped with gauze sponges. No attempt is made to dilate the nasofrontal duct or open any of the anterior ethmoidal cells.

The wound is left open, but not packed with gauze. For the first 24 hours the opening is maintained by soft rubber tubing or a roll of gutta-percha tissue. After this the wound is kept open by touching the edges with carbolic acid three or four times a week. When used with care none of this acid gets into the sinus. In this way the wound may be kept open as long as necessary, the granulations are kept down and the danger of secondary infection with skin organisms is reduced to a minimum. If tubing or a drain of any kind is left in the sinus for longer than 24 hours it becomes encrusted with secretions and encourages the formation of granulations. If either tubing or drains are removed and fresh ones replaced at each dressing, it is not only a painful procedure, but encourages secondary skin staphylococcus infection of the sinus.

The sinus is irrigated with hot sodium chloride solution at each dressing, and the frequency of the dressings depends on the amount of discharge. Sometimes it is necessary to change the dressings several times a day for the first three or four days. The dressings should be painless. A painful operation under local anesthesia or a painful dressing is evidence of poor technique. The apparatus for irrigating the sinus is simple. The glass part of a straight medicine dropper is connected with a Chetwood or a rubber ear syringe by three or four inches of soft rubber tubing. During the irrigation the patient either sits upright or lies on his side. For the first few days the irrigating fluid returns through the external wound: at any time from the third to the seventh day after operation the fluid begins to come out

through the nose. After a few days of free through-and-through irrigation of the sinus it is safe to cover the external wound with dry gauze and allow it to close. In addition to these treatments of the frontal sinus it is necessary to keep the nasal passages clean with suction, and if transillumination or X-ray indicates an infection of the antrum, it also should be irrigated daily until clear.

Most of our 36 patients have been sent to the hospital from one to three weeks after the onset of acute frontal sinus symptoms. All but one recovered without complications. This patient developed a suppurative parotitis and a *Staphylococcus albus* septicemia on the second day after operation. Multiple abscesses appeared on the face, scalp, scrotum and fibula, and on the 40th day osteomyelitis of the skull set in. He finally recovered and has been well during the past year.

Theoretically the dangers of this operation are infection of the marrow spaces and osteomyelitis of the skull. Only one of our patients had osteomyelitis and that followed a suppurative parotitis and septicemia. We feel that the danger of spreading the sinus infection by external incision and drainage is much less than the danger of converting an acute into a chronic frontal sinus infection that will require much more radical surgery to cure.

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XXXVI

MANAGEMENT OF CAVERNOUS SINUS THROMBOPHLEBITIS

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SYRACUSE

The title of this paper may be presumptuous. A year ago it would have been without meaning. Today, however, with the knowledge of the advances made in chemotherapy in 1940, we suggest that there can be a planned management for cavernous sinus thrombophlebitis. When further advances in chemotherapy come to our attention, as they surely will, what is said here will then seem inadequate. Yet the suggestions of the hour are as daylight compared to the night of despair which surrounded most of us in the past when we were confronted with one of these cases.

Before proceeding further we wish to state that we will confine our discussion to the anterior fulminating type of cavernous sinus thrombophlebitis. It is usually caused by an infection which invades the cavernous sinus by way of the ophthalmic veins. On occasion, the infection reaches the sinus by way of the pterygoid plexus. The acute fulminating type differs considerably from the so-called "chronic compensatory" type described by Eagleton.[1] (The term "chronic" is a misnomer for it is chronic only in the sense that the cases of this type live longer, usually, than those of the fulminating group.) The term "chronic compensatory" applies to those cases in which there is a thrombosis of the cavernous sinus, which has developed by a retrograde process from the vessels communicating with the cavernous sinus. In many of these there is only a cavernous sinus thrombosis and not a true cavernous sinus thrombophlebitis. In fact, the clot in these instances may be sterile. Grove,[2] in perhaps the best review of this subject in the literature in recent years, brings out this differentiation nicely.

After reviewing the routes of infection Grove states that sterility of the clot has much to do with the likelihood of recovery. After mentioning the oft-quoted statistics that recovery from all

types of cavernous sinus thrombophlebitis is probably not greater than 7%, he gives as his opinion that "in septic types with infection reaching the sinus via afferent vessels, the mortality is practically 100%." (It should be noted that this article was written before the discovery of the sulfonamides.) He also mentions that it is his judgment that in cases of recovery from cavernous sinus thrombophlebitis most of the thrombi are sterile, and he suggests that a review of the literature to that time (1936) shows that the percentage of recoveries in patients operated upon is less than in those not operated upon. These opinions, to us, exhibit sound reasoning based on known facts. They are mentioned because they are definitely related to the subject at hand. Case management of cavernous sinus thrombophlebitis with a sterile clot would certainly differ from the management of one with a present and continuing infection. With the same management there might be a totally different result. This is the *bête noir* of all therapeutic discussions. On the other hand, if the subject is limited to the type which (before the discovery of the sulfonamides) has been practically 100% fatal, then any good result from therapy has some significance. It is for this reason that our discussion will be limited to the anterior fulminating type.

The origin of anterior fulminating cavernous sinus thrombophlebitis is usually due to lesions about the upper lip and the nose, and in the great majority the infecting organism is the staphylococcus. Other infective agents can and do invade the sinus, but it is usually the staphylococcus. Scarpellino, Stookey and Hall,[3] discussing the pathogenesis of cavernous sinus thrombophlebitis in a very excellent article, state that "pathologically, in order for a thrombus to form inside a vessel three factors must interplay; namely, there must be (1) damage to the intima of the vessel wall; (2) a change in the coagulability of the blood plasma; (3) a slowing of the blood stream.

"Anatomically the cavernous sinus is a widened part of a venous blood channel which is divided by trabeculations. The widened channel and the spongy nature of the sinus both serve to retard the blood flow, consequently the hydrodynamics and lack of valves favor blood flow retardation."

These authors injected a series of 25 rabbits using the ear as the site of injection, with staphylotoxin. In these "the intima of the vessels show swelling of the lining endothelial cells, and the blood vessels are intensely engorged and dilated, and round balls of red cells are seen clinging to the walls of the dilated veins covered by a rather structureless limiting membrane of fused platelets or granular

fibrin. The vessel wall upon which this spherical mass rests has lost its staining properties and is not being invaded or repaired by new or potential fibroblasts."

They report six cases of human cavernous sinus thrombophlebitis with the recovery of staphylococci in each. A filtrate produced from these cases showed the property of hemolyzing red blood cells, of producing necrosis and forming thrombi when injected in the marginal veins of the ear of a rabbit. They feel in staphylococcic infections the damage is done by a toxin elaborated by the metabolism of the bacteria. They add, "When the clinician has the opportunity to observe, at post mortem, the cavernous sinus filled with a septic thrombus and the contiguous portion of the sphenoid bone and the hypophysis to be partially liquefied by the lytic influence of the toxin together with the coexisting evidence of widespread septicemia with innumerable abscesses in the lungs, septic infarcts in the kidneys and frequently thrombi in the large vessels throughout the body, he is overwhelmed with the hopelessness of any therapeutic procedure." They discuss the possible use of staphylococcic antitoxin but suggest that it can only be of use in neutralizing the circulating toxin in the blood and will not influence the toxin already bound irreversibly to the tissue cells which has caused irreparable damage and which no amount of added antitoxin can influence.

For this serious pathological picture various methods of treatment have been advocated. They fall into three categories; surgical, bactericidal, and chemotherapeutical. It is difficult to evaluate the worth of these procedures to any degree of accuracy, for in each of these classifications cases of the "chronic compensatory" type have been included. The promise of the future undoubtedly lies with the use of chemotherapy, but credit must be given to the pioneers who sought a cure for this condition. To the surgeons in particular we owe much. Their work, while not notably successful, has led to a better understanding of this condition, and, as will be suggested later, their methods may still prove to be of some value. With this in mind a summary of the surgical procedures which have been advocated is presented.

The first surgical attempt recorded was made by Bircher[4] in 1892 when he approached the cavernous sinus via the temporal route. The patient recovered. There is some question as to the diagnosis, even though the procedure of reaching the sinus and placing a gauze drain in the posterior end was carried out. In 1899 Dwight and Germain[5] recorded their intradural temporal approach. They incised

the sinus and removed the clot. In 1905 Luc[6] advocated the transantral route. He entered the antrum of the opposite side and passed from this through the sphenoid to its lateral wall and thus reached the cavernous sinus. About the same time Langworthy[7] reported four cases reached by way of an intranasal approach. In 1914 Mosher[8] wrote of his orbital approach. He advocated enlarging the sphenoid fissure by cutting away part of the orbital plate. In 1926 Eagleton added to Mosher's orbital approach by taking off part of the great wing of the sphenoid and ligating the internal carotid. We were unable to discover to whom should be given prior credit for the suggestion of ligation of the afferent vessels of the cavernous sinus. We could find no case in which a recovery was reported where reliance was placed on this method alone. Browder and Myerson[9] reported what might be classed as a variation of this procedure when in 1935 they operated for prevention of cavernous sinus thrombophlebitis by exposing the anterior end of the cavernous sinus and used electro-coagulation to sever the relation of the ophthalmic veins to the sinus. The patient recovered but suffered the loss of vision in that eye.

The use of various bactericidal agents (sera, phages, etc.) for cavernous sinus thrombophlebitis has not been very successful in bringing about recoveries. We could find but four cases where this was the method of choice. Undoubtedly these substances have been used in many instances, and the scarcity of reported recoveries is therefore noteworthy. With only four reported recoveries it may be fair to suggest that these recoveries might have taken place without the use of these aids.

Since the discovery of sulfanilamide the literature on this subject has taken on new interest. Cavenagh and Oxon[10] made a critical study of reported recoveries prior to 1936 and could find only seven cases of the anterior fulminating type which seemed to fill the requirements of a true cavernous sinus thrombophlebitis that recovered. From 1936 to date (March 15, 1941) there have been nine reported recoveries. Amongst the nine is the one reported by Seydell.[11] His case, from the description, was not of the anterior fulminating type, inasmuch as the infection was from a lateral sinus following mastoid infection, and therefore should not be included in a list of recoveries of patients whose cavernous sinus thrombophlebitis is of the type under discussion. MacNeal and Cavallo[12] reported a recovery with the use of sulfanilamide but used also antistreptococcus serum. Goldenburg[13] used sulfanilamide, as did Barnshaw[14] and Pace.[15] Morrison and Schindler[16] were the first to report

success with the use of sulfapyridine; Wolfe and Wolfe[17] in January of this year report the first recovery with the use of sulfathiazole. In the same month Champ Lyons,[18] reporting two cases in which the patients recovered, added to sulfathiazole the use of heparin. Heparin, which has the power of reducing the coagulation time of the blood, was added to the treatment of these two patients to prevent extensive thrombosis and thus afford the sulfathiazole an opportunity to do its work. In the first of the two cases, that of a female of 31, the total dosage of heparin was 225,000 units. That it was a fulminating case is shown by the fact that meningitis was still present on the 49th day of the illness. This patient was not discharged until the 67th day of her illness and even then had a partial third and complete sixth cranial nerve paralysis. The second of the two cases was that of a male of 41. The total dosage of heparin was 580,000 units. Lyons came to three conclusions as a result of his experience with the use of heparin and sulfathiazole. (1) Ten days of treatment were necessary before one could be reasonably assured of a possible happy outcome. (2) Blood sulfathiazole must be maintained at a 5 mg. per cent level in order to control meningitis if present. (This differs somewhat from the earlier literature on sulfathiazole which stated that the drug was not secreted effectively in the spinal fluid. See also the report of our first case below.) (3) Heparin prevents extension of septic thrombosis thereby destroying the method of advance in staphylococcic bacteremia.

These results herald the dawn of a new day in the treatment of cavernous sinus thrombophlebitis. We can all rejoice, for here is some promise that we need no longer expect a mortality of nearly 100% in these cases. It is indeed a happy prospect. But a disturbing note must be sounded. With the coming of this new chemotherapy the day of certainty in diagnosis is passing. When the cases proved fatal and autopsies were obtained, one could say with certainty whether or not cavernous sinus thrombosis was present. When a so-called cure is established, that certainty is gone. As yet there has been no method devised to prove clinically one way or the other that a thrombophlebitis of the sinus exists. True, most of these reported cures fulfill the criteria for diagnosis as set up by Eagleton. These are: (1) a known site of infection; (2) evidence of infection of the blood stream; (3) early signs of venous obstruction in the retina, conjunctiva or eyelid; (4) paresis of the third, fourth and sixth nerves, resulting from inflammatory edema; (5) the formation of an abscess in the neighboring soft tissues; and (6) evidence of meningeal irritation. Even with these criteria fulfilled however, there can be no proof that the cavernous sinus has been

thrombosed. Further, as medication improves and methods of application are bettered, fewer of these criteria will appear in reported recoveries. What we are saying then is this: a new day in the treatment has come, but until newer diagnostic measures are available, the authenticity of reported recoveries will have to be based on clinical rather than purely scientific grounds.

REPORT OF CASES

We treated two cases of cavernous thrombophlebitis in 1940. One resulted in a fatality, the other in a cure. A summary of their histories follows.

CASE I.—E. S., a 14 year old boy, on July 9th discovered a small pimple on the left side of the nose. The next day his mother pricked the furuncle with a needle which she had previously "sterilized". There followed some redness and swelling of the nose, a low fever and some general malaise.

On July 13th, the patient had a chill and fever rose promptly to 104°. This was followed by frontal and supraorbital headache. He was admitted to the hospital. At this time there was swelling of both eyes, more marked on the left, and swelling of the forehead in the midline.

On July 14th, there was fixation of the eyes and the patient complained that he could not see when the lids were retracted. There was now marked swelling with closure and with this, marked conjunctival edema. The ophthalmological report showed dilatation of the retinal veins and blurring of the nasal margins of the optic discs. There was disorientation with question of a stiff neck. A spinal puncture was done and an initial pressure of 256 mm. of water was obtained with a clear fluid. No growth was obtained from this puncture.

On July 15th the patient was comatose. Blood culture revealed a *Staphylococcus aureus* bacteremia. The patient had previously been on sulfanilamide therapy. He was promptly switched to a sulfamethylthiazole regime. (Sulfathiazole was not available at the time.) He was given in all 64 gm. of this drug. Fluids and medication had to be given by Lavine tube through the nasal passages. Spinal fluid taken in the evening showed 143 cells and subsequently *Staphylococcus aureus* was recovered from it.

The condition of the patient did not improve with this therapy and the addition of appropriate supportive measures. He died suddenly on July 21st, of respiratory failure. While the blood culture never became negative, it is very interesting to note that no spinal fluid taken after July 18th showed bacterial growth.

Autopsy showed both cavernous sinuses to be filled wtih reddish brown to reddish yellow thin purulent fluid. No thrombi were found in the cavernous or intercavernous sinuses. There were some in the terminal veins along the floor of the skull. There was some basilar meningitis. The lateral wall of the left sphenoid was necrotic, and this sinus was filled with purulent material similar to that found in the cavernous sinuses. The pituitary was diseased; it showed a superficial necrosis.

COMMENT

The boy lived nine days with the treatment as outlined. It was the longest survival either of us had seen. The autopsy showed complete lysis of the thrombi in the two cavernous sinuses. Yet the thrombophlebitic process had continued on into the communicating veins.

Reconstructing our therapeutic plan, we decided that in the future we would employ the use of some anticoagulant, continue the use of the sulfonamides and perhaps, if the patient lived a goodly number of days but was not doing well, resort to surgical drainage of the cavernous sinuses.

It was only a few months after this that one of us (I. H. B.) had a patient, seen in consultation by the senior author, a summary of whose history follows.

CASE II.—On December 9, 1940, M. B., a female 22 years of age, presented herself with a story of headache and tenderness of the left nasal vestibule. She had on examination a furuncle at this site, which ruptured spontaneously two days later, from which a culture of *Staphylococcus aureus* was recovered. On December 10th there was fever of 101°, edema of the left lower eyelid, pain in the left cheek and the root of the nose and an increase in headache. She was admitted to the hospital. Sulfathiazole was started and given throughout her illness save for one short interval. A total of 106 gm. was given, and the sulfathiazole level in the blood was maintained at an average of 8 mg. %.

On December 12th, the swelling had increased and the angular vein could be palpated. Surgical consultation was sought, and after considerable discussion it was agreed that ligation was not advisable. It was thought that if the vessels could be palpated a clot was present, and its advance would be beyond any surgery short of attack upon the cavernous sinus. At this point the procedure of Browder and Myerson might conceivably have been of service. It seemed too radical, for the patient was apparently doing reasonably well; the temperature was not high, there had been no chills and as yet the left eye had not become swollen shut, nor had conjunctival edema set in.

On December 13th, however, the picture suddenly changed. At 6 A.M. the patient had a chill, the temperature rose to 103.8°, the left eye shortly thereafter was closed, and the right eye became swollen. Ophthalmological consultation a little later in the day showed both discs with blurred margins and the veins and arteries markedly dilated. The eye examination was repeated at least twice daily for the next ten days. With this evidence of beginning cavernous sinus thrombophlebitis, heparin, administered by continuous intravenous drip, was added to the sulfathiazole therapy. It was given in 4% strength. This is equivalent to eight units of heparin per cubic centimeter of intravenous fluid. According to the needs of the patient the vehicle used was physiologic solution of sodium chloride, 5% dextrose solution of lactated Ringer's solution. The intravenous solution was allowed to run more rapidly, or the flow was retarded according to the reading of the coagulation time of the blood, which was tested every four hours. This reached a peak of nearly five hours within 24 hours of the start of the administration of the heparin. The flow of the fluid was varied to maintain an approximate

level of two hours' coagulation time. In all a total of 129,000 units of heparin was administered.

Within 24 hours of the start of the heparin therapy the swelling of the eyes began to recede. There was thereafter a gradual return to normal which paralleled a similar return to normalcy of the retinal veins and arteries. This took a little over a week.

After two days of the heparin therapy the urine began to be cloudy. This increased till the urine was bloody and then clotted blood was passed. Despite daily transfusions the blood level lowered to an alarming degree. The furuncle of the nose bled from both the inside and outside. There was swelling of the elbow joints and some others, suggestive of hemorrhage into them. Considerable ecchymosis was evident. With these conditions present the heparin and sulfathiazole were discontinued on the ninth day. (Sulfathiazole crystals have been found in the urine and have caused bleeding from the kidneys. No crystals were found in this case.) Within 12 hours there was a sharp rise in temperature following a chill, and the sulfathiazole was started again. Inasmuch as the eye grounds were now normal and the swelling in the eyes had about disappeared, we did not add heparin to the sulfonamide therapy. Five days later the temperature had fallen to normal by lysis. During the course of her illness, the patient's skull was x-rayed at weekly intervals. These showed a hazing of the left petrous ridge in the region of the superior petrosal sinus. Blood culture was repeatedly sterile. There was no indication at any time for lumbar puncture. The patient was discharged as well on the 30th day of her illness.

It is impossible to say, as it will be in many similar cases, whether or not cavernous sinus thrombophlebitis was present. We believe it was. The promptness of the therapy prevented the appearance of the more serious symptoms of this condition. Heparin was started within five hours of her initial chill. It is rare that such an opportunity as this presents itself. Usually we are not called into consultation in these cases till the condition has been present, fully developed, for 24 hours or more. In this case the patient was under our eyes, so to speak, from the very beginning. It was dramatic to see the picture develop. It was equally dramatic to see the effects of the therapy. We do not deny the possibility that sulfathiazole alone might have brought about an equally happy result, but sulfathiazole was used prior to the initial chill and did not prevent a spread of the infection. It has seemed to us that in this particular case the combined therapy was a life-saving procedure.

FUTURE MANAGEMENT

In the light of these two cases and the evidence given above, our future mode of procedure will be along the following lines:

1. To start treatment early. Of course, this is not always possible. We must continue to preach prevention and stress the importance of making an early diagnosis.

2. To discard ligation. By the time one decides that this procedure is necessary the infection is beyond control by ligation. Batson,[19] in discussing Barnshaw's case of recovery, reviews this

aspect. Collateral circulation, even after multiple ligations, he states, can carry the infection to the cavernous sinus.

3. To seek ophthalmological consultation early and often. Benedict[20] and Walsh[21] stress its necessity. Benedict states that frequent examination of the fundus in a suspected case is more valuable than a single examination. He urges we follow the example of Patton who taught that the eye should be examined every three hours.

An ophthalmological examination is of great value in the diagnosis of cavernous sinus thrombophlebitis. Its employment in conjunction with the use of heparin may be additionally helpful. Given a case in which progress is satisfactory, a return of the retinal vessels to their normal size would indicate a probable canalization of the thrombus by the lytic process of the toxin of the staphylococcus. This would be, it seems to us, the proper time to discontinue the use of heparin, even though it might still be necessary to continue the administration of one of the sulfonamides.

4. To determine, if possible, the causative organism and administer the appropriate sulfonamide drug. If the causative organism cannot be determined, sulfathiazole should be used, as in the very great majority of acute fulminating cavernous sinus thrombophlebitis cases, the invading organism is the staphylococcus.

5. Along with the sulfonamide to start heparin, in large doses at first to reduce the coagulation time of the blood as soon as possible, and then regulate the amount to maintain a two-hour level for the coagulation time.

Continuous intravenous therapy for over a week or more is a severe trial for any patient, let alone one who is as sick as these patients are. The use of a ureteral catheter tied into a vein is a suggestion which we are inclined to follow in another case. It would allow freedom of motion not otherwise obtainable.

6. To watch the blood, the urine and the spinal fluid for evidence of infection. To treat accordingly.

7. In those cases in which progress is not satisfactory, to be alert to indications for surgical interference. This should not be delayed too long. In the first case above, osteomyelitis of the sphenoid bone had taken place in the nine days of the illness, and a necrosis of the pituitary was observed. In fatal cases the latter is of no consequence, but in those that live this may be of considerable moment. During the year 1940, in Syracuse, beside the mention just made, there were two fatal cases of cavernous sinus thrombophlebitis

in which autopsies revealed disease of the pituitary. In one there was total destruction, and diabetes insipidus was in evidence prior to death. Walsh, and Scarpellino, Stookey and Hall, mention the frequency of pituitary involvement. For this reason, and the fact that sulfathiazole may not sterilize an abscess of the sinus formed from a liquefied clot, surgery may be a necessary therapeutic procedure. Heparin would have to be discontinued during and immediately following operation, but inasmuch as the blood coagulation time returns to normal within about four hours after its discontinuance, its use is not contraindicated till just before operation. In view of the control we now have of pyogenic infections, the wide exposure of former days is not required. It does not seem that sacrifice of an eye is essential although that procedure had its place before the advent of the sulfonamides. The nasal approach of Langworthy seems to us to meet the requirements of drainage should this be necessary.

SUMMARY

A discussion of the acute fulminating type of cavernous sinus thrombophlebitis, with its reported recoveries before and after the advent of the sulfonamides and its past management, both surgical and medical, has been presented. Two cases have been reviewed. In the light of this information a suggested scheme of management has been outlined. This includes ophthalmological consultation, the use of the appropriate sulfonamide, the addition of heparin, the employment of proper supportive measures, and the resort to surgery if this is found necessary.

Medical Arts Bldg.

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XXXVII

THE IMPORTANCE OF RECOGNITION OF ALLERGIC CONDITIONS BY THE RHINOLOGIST

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Although a relationship exists between all medical and surgical specialties, possibly this relationship is best demonstrated in that existing between the present-day treatment of allergy and otolaryngology. A competent otolaryngologist must either himself be equipped to carry out allergic investigations, or he must call upon a trained allergist to secure the information necessary to prescribe and direct treatment in allergic cases. The latter arrangement is usually more desirable, for these investigations must be done with extreme care, and require an amount of time and experience which the average otolaryngologist does not possess. Although all allergists should be trained internists, the converse is not true. Too many general practitioners and pediatricians dabble in allergy. The result is haphazard and incomplete allergic studies which are worthless, serving only to confuse the issue, unless responses are most obvious.

With the exception of acute and chronic infections allergy is the most common affection of the nose and paranasal sinuses. These cases seek the rhinologist, and he must be able to recognize, or at least suspect, the allergic condition, and on him rests the responsibility of seeing that steps are taken to have the patient properly treated. Unfortunately many rhinologists still cling to repeated local treatment of these cases, which rarely results in anything more than temporary relief.

The typical allergic nose with its pale, boggy, swollen mucosa, excessive mucoid discharge, and a tendency to resist shrinkage, is not hard to recognize. There are many gradations, however, between this extreme and the normal nose. Many early allergic noses of moderate degree defy recognition on inspection alone. They may show the redness of an acute or subacute coryza. Here the study of secretions for eosinophiles is of value. Then, too, there may be an infection superimposed upon an allergic condition which clouds the allergic picture. In these cases repeated examinations must be carried

out so that an estimate of conditions upon subsidence of the infection can be secured.

The rhinologist must secure a careful history in all patients suspected of allergy. This history should not be confined to nasal symptoms alone, but should take into consideration the possibility of allergic manifestations of other types. Studies of large series of cases have shown that only 30% of those with symptoms of nasal allergy show no other symptoms of an allergic nature. Therefore in 70% one should expect asthma, skin conditions, gastrointestinal symptoms, or allergic headaches to complicate the clinical picture. One, therefore, has a right to expect allergy to show itself in multiple rather than single clinical forms. Although the patient presents himself for relief of his most obvious symptoms, associated manifestations of the condition must be sought for and not overlooked.

For convenience, it may be helpful to classify these cases seeking help from the rhinologist as:

1. The suspected allergic.
2. The definite allergic without demonstrable sinus infection.
3. The definite allergic with sinus infection.
4. The definite allergic with polyposis.
5. The definite allergic with polyposis and sinus infection.

It is justifiable for the rhinologist to keep the suspected allergic under observation long enough to determine that he is or is not dealing with a low grade non-purulent type of infection. This having been determined and infection ruled out, steps should be taken to secure a proper allergic survey.

The second group of definite allergics without demonstrable sinus disease, should usually at once be referred to the allergist. To do otherwise is most often a waste of time. Sometimes if the history of contacts is definite, results can be secured by the removal of obvious offenders, such as feather pillows, cats, dogs, horses, face powder, etc. Cases where such simple withdrawals are without benefit demand the usual careful estimation of their allergic status.

The definite allergic with sinus infection will usually require allergic study. Often anti-allergic therapy is of signal advantage in aiding the rhinologist to clear up this infection. Sometimes treatment of the sinus condition alone secures results, so that it is justi-

fiable to try such therapy for a limited time before securing the allergic survey.

Where pedunculated polyps are found, they must be removed. Not infrequently so much relief follows this procedure that further steps are unnecessary. If the polyps are sessile or improvement does not follow the removal of the larger pedunculated variety, one should secure allergic studies.

Patients showing both polyposis and sinus infection demand the removal of polyps and treatment of the sinus disease. Here again, allergic study and treatment is practically always indicated, and may be of great value to the rhinologist in his efforts to clear up this infection.

In the majority of these cases of all groups the roentgenograms show clouding or thickened lining of all or at least some of the sinuses. The roentgenologist reports multiple sinus disease, and the patient and frequently the internist demand to know why this is not being eliminated. True enough this clouding of the sinuses may be the result of infection, but often it is simply a swelling of mucosal lining similar to that which takes place in the nasal cavity. It is absurd for us to expect the profound swelling seen in the nasal cavity to stop at the sinus ostia and not involve the mucosa of the sinuses themselves, which after all are simply invaginated parts of the same structure.

Among the laity sinus surgery has a bad name. Rhinologists have not yet lived down the atrocities performed under the name of needful surgery in a previous generation. This need not be so. If careful selection and analysis is made of all our sinus cases, and operation performed only on those that really need surgery, the results are uniformly gratifying to both patient and physician. Many of these chronic cases require surgery, but it is not emergency surgery. All permit time for study and an attempt to secure results by anti-allergic measures administered by the allergist and conservative treatment on the part of the rhinologist. If there is bad nasal anatomy or large obstructive polyps or turbinates, it is almost certain that allergic treatment will fail until these conditions have been corrected. Best results, however, are secured where the allergist and rhinologist talk the matter over and together decide upon the procedure of choice.

Too often anti-allergic therapy fails to secure satisfactory results. In the minds of many patients and physicians these failures condemn

the whole procedure. There are, however, enough successes, in full or in part, to more than justify the continuation of allergic studies and treatment. There are certain things worth trying in the attempt to relieve those individuals who in spite of all efforts remain wretched and partly incapacitated with blocked and discharging noses. The measures most likely to secure results all have as their goal a desensitization of a considerable portion of the nasal mucosa. The use of the galvanic current passed through some electrolyte in the nasal cavity is not looked upon with favor, although many satisfactory cures have been reported. Such treatment distributes its cauterizing effect generally throughout the nasal cavity, often resulting in permanent anosmia. The same result can be secured in other ways without interfering with the olfactory areas. Electrocoagulation, the galvano-cautery, the injections of solutions such as alcohol, quinine and urea, and sodium morrhuate have all been used. One of the simplest and most satisfactory procedures is the application of the chromic acid bead, or a 30% solution, to the mucosa of the inferior and lower edge of the middle turbinate. Phenol and trichloracetic acid so applied can be used, but they produce less marked and prolonged effects. The chromic acid treatment may produce a severe reaction lasting from three to ten days with considerable exaggeration of symptoms. Almost invariably the patient is then improved or free of symptoms for a period of time varying from a few weeks to many months. In spite of the possibility of securing results by the above procedures, the nasal mucosa should not be subjected to these relatively harsh measures unless anti-allergic therapy has failed.

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XXXVIII

THE MIDDLE EAR AND ACCESSORY NASAL SINUSES FROM A FLIGHT SURGEON'S POINT OF VIEW

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Since the days of the First World War, interest and development in aviation have increased by leaps and bounds. The rapid expansion of aviation in the past two years and that planned for the near future probably surpasses anything previously dreamed of by even the most ardent supporters of aviation. The specialty of aviation medicine has developed along lines closely parallel with the development of aviation itself. This sequence of events made it necessary for medical examiners in aviation medicine to develop new methods and revise old methods for diagnosis and treatment.

With the advent of flying, man began to suffer the stress of poor anatomical compensation for his new and unusual environment. In this relation, I shall limit my discussion to the nose and middle ear.

The middle ear and accessory nasal sinuses are air-filled cavities. The eustachian tube, a small potential tube 34 to 36 mm. in length, connects the tympanic cavity with the nasal part of the pharynx. The nasal sinuses open into the nose by relatively shorter passages and larger openings. By means of these openings the cavities are drained and aerated and any difference in atmospheric pressure inside and outside the air cavities is equalized. These air cavities are lined with mucous membrane which is continuous with the mucous membrane of the nose, and readily becomes swollen from congestion, inflammation, or trauma, thus closing off the air cavities from the nose.

The flyer's chief trouble with the middle ear and accessory nasal sinuses is due to the failure of the pressure within the cavities to become equalized with the changes in atmospheric pressure on ascent or descent. The atmospheric pressure becomes less as the flyer ascends. For instance, at 16,000 feet the atmospheric pressure is approximately 420 mm. of mercury, as compared to 760 mm. of mercury at sea level. If, for any reason, the pressure is not equalized

between the air cavities of the nose and middle ears and the outside atmospheric pressure on ascent from sea level to 16,000 feet, there would be approximately 360 mm. greater pressure in the air cavities of the ears and nose than on the outside. What is more common, however, is normal ventilation on ascent but none on descent, and here there would be approximately 360 mm. of pressure more on the outside than within the air cavities. This greater difficulty on descent is due to the fact that, as the pressure on the outside becomes greater, it presses the slit-like opening of the eustachian tubes closed, thus preventing the air from entering the middle ear by its own pressure.

In examining pilots and prospective pilots, one should always keep in mind the air cavities of the nose and ears. There should be no obstruction or any condition which might cause an obstruction to the passage of air to and from the sinuses and to the middle ear. The following conditions should be looked for: deviation of the nasal septum, nasal allergy, polyps, tumors, and acute or chronic infections of the mucous membrane of the nose or sinuses. Particular attention should be paid to the patency of the eustachian tubes. In addition there should be no tendency to swelling of the mucous membrane as in vasomotor rhinitis.

Fortunately, in comparison with the middle ear the accessory nasal sinuses have relatively shorter passageways and larger openings into the nose. Therefore, the formation of a pressure difference between the sinuses and the outside atmosphere is less common than in the ear. The pain experienced from unequal pressure is often quite severe, but it is quickly relieved and the trauma is less marked.

Pressure difference between the air in the tympanic cavity and the outside atmosphere as a result of the change of altitude during airplane flights causes a traumatic condition of the middle ear known as aero-otitis media.

ETIOLOGY

Aero-otitis media is due to the failure of the eustachian tubes to open during changes of altitude in airplane flights. Failure to open the eustachian tubes voluntarily may be due to being asleep, to unconsciousness or to ignorance of the need to open the eustachian tubes on the part of the passenger or to carelessness on the part of the pilot. Inability to open these tubes voluntarily is quite frequent. Some of the common causes of this deficiency are stenosis of the tubes, deviated nasal septum, vasomotor rhinitis, nasal allergy, polyps, sinusitis, tonsillitis, tumors in the nose, paralysis of the soft palate or

of the pharyngeal muscles, acute or chronic inflammatory conditions of the upper respiratory tract, trauma from the adenotome or curette during adenoidectomy, and malposition of the jaws.

Slight positive pressure produces a sensation of fullness in the ears. As pressure increases tinnitus develops. Still higher pressure produces severe pain in the ear which may radiate to the temporomandibular joint and the parotid gland. Deafness is marked and may be associated with vertigo and nausea. The deafness clears rapidly and usually disappears within one to three days, although the tinnitus may last much longer. Negative pressure produces the same symptoms but is never relieved through its own force. The objective symptoms depend on the amount of damage done. If the trauma is slight, there will be a little injection of the tympanic membrane especially around the malleus. If a pressure difference still exists there will be a retraction or bulging of the tympanic membrane, depending on whether there is a decreased or increased pressure inside the middle ear. A positive pressure is shown by bulging of the ear drum with a decrease or absence of the light reflex. In decreased pressure there is a retraction of the drum with a marked prominence of the short process of the malleus. The drum is inflamed and varies in appearance from a slight injection in mild cases to an intense redness in severe cases, in which the injection is most impressive. Without knowing the history of the case, it is easy to mistake this condition for acute infectious otitis media. We would expect acute infectious otitis media to occur quite often in flyers due to the air rushing into the ear from the nose, carrying the infection in. However this condition occurs infrequently. Rupture of the ear drum may occur from positive or negative pressure difference in the tympanic cavity. The rupture is usually a linear tear and may occur in any portion of the drum. It is often quite extensive and may be accompanied by bleeding. When actual traumatic inflammation occurs, a serous transudate often collects in the tympanic cavity. Here we see a similarity to the condition known as otitis media serosa or ex vacuo. This exudate rapidly disappears, usually within 24 to 36 hours after removal of the pressure difference.

In older pilots we often see a chronic condition of the ear characterized by thickening and retraction of the ear drum with prominence of the posterior maleolar fold and of the short process of the malleus with indrawing of the umbo. The light reflex is diminished or absent. There may be a sense of fullness in the ears and some loss of hearing. An audiogram shows a hearing loss for low tones. This is a form of conduction deafness. The reaction to the Rinne test is

negative. This condition is usually more marked in fliers who give a history of having had trouble all along ventilating their ears, and is exaggerated by flying and by upper respiratory infections. In considering the amount of abuse the ears receive, it is remarkable that there is such a small amount of hearing loss found in pilots even after 15 or 20 years of flying.

TREATMENT

Prophylaxis is important. Pilots and other flying personnel should be tested for patency of the eustachian tubes. Those who suffer from stenosis of the eustachian tubes, either permanent or temporary, should not be allowed to fly except under controlled conditions, such as gradual changes of altitude and low altitude flying. In flying it is most important to instruct the individual concerned with explanation of the functioning of the eustachian tubes and simple methods of ventilating the tympanic cavity. As long as ventilation of the middle ear is under voluntary control, there is little reason for one in commercial aviation to suffer any difficulty in changes of altitude. Ordinarily an individual swallows once every 60 to 90 seconds. Of course the normal rate of swallowing would do little good in dive bombing or dive attack maneuvers such as the Nazis have been using in their Stukas and Messerschmidts. On dives these planes attain enormous speeds. This is easily understood if we realize that the plane descends from an altitude of 8,000 to 10,000 feet to within 500 feet of the ground in from 15 to 20 seconds. In spite of a continuous yell which the pilot starts as he enters his dive or of continuous swallowing, quite often the tympanic membrane is ruptured. If such is not the case repeated dives over short periods of time will almost inevitably lead to aero-otitis media. In a blackout or near blackout the flyer may lose voluntary control over aeration and cause damage to the ears in this way. Accumulation of pressure difference in the ears stimulates a desire to swallow more often than normally. The easiest method of ventilating the tympanic cavity is by swallowing, and this should be recommended. Other methods are yawning, shouting, or by contracting the salpingopharyngeal muscles. Pilots should be grounded during acute upper respiratory infections. The older pilots have learned from past experience that respiratory infections predispose to the occurrence of aero-otitis media, and they will voluntarily remain on the ground until they have recovered.

Relief of pain is of first importance. It may be necessary to give morphine. Warm topical applications to the ear drum are

soothing and beneficial. Dry heat is also quite good. If the drum indicates that a pressure difference exists, the area around the opening of the eustachian tube should be treated with adrenalin or other astringents, and the tympanic cavity gently inflated by Politzer's method. Hot gargles, astringent nose sprays and steam inhalations should be recommended for symptomatic relief. If the condition does not clear up in two or three days, acute or chronic bacterial infections, stenosis or other causes should be looked for and removed.

SUMMARY

1. With the increase of interest in and the development of flying, aviation medicine has become a specialized field.

2. The middle ear and accessory nasal sinuses are affected by the sudden changes in atmospheric pressure resulting from rapid ascent and descent.

3. Examination of prospective pilots should always include a thorough inspection of the ears, nose and throat in order to discover the existence of any pathological conditions.

4. Aero-otitis media is a pathological entity which results from rapid changes in altitude, where inadequate ventilation of the tympanic cavity occurs.

5. Aero-otitis media can be prevented where no pathological obstruction of the eustachian tube exists by the simple methods of swallowing, yawning, shouting, or contraction of the salpingopharyngeal muscles.

XXXIX

THE PRESENT STATUS OF ROENTGEN THERAPY IN SINUSITIS*

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Osmond, in 1923, was probably the first to direct attention to the beneficial effect of roentgen irradiation in the treatment of sinusitis. An observation which he made as early as 1916 may be said to form the basis of the modern roentgen therapy of sinusitis. To quote from Osmond's article, "The attention of the writer was called to this subject when patients were relieved from pain in the forehead for a time after the making of radiograms for the diagnosis of a suspected frontal sinusitis." It has been the common experience of radiologists that patients are frequently relieved of their symptoms, especially pain, following a roentgen examination of the paranasal sinuses. This has also been observed in acute mastoiditis. Clinicians referring the patient will often bring this observation to the attention of the roentgenologist. Many patients thus examined are under the impression that they have received some form of electrical treatment, not realizing that the procedure has been done solely for the purpose of establishing a diagnosis.

Although 18 years have elapsed since the publication of Osmond's article, it has been only within recent years that much attention has been given to the possible role of irradiation in the treatment of sinusitis. The general medical profession is almost wholly unaware of this form of therapy for sinus disease, and only a few rhinologists have been sufficiently interested to inquire into the subject. This is but a natural reaction of the medical profession to the unscientific and unwarranted claims that have been made for roentgen therapy in the treatment of every conceivable ailment of the human race, from falling hair to fallen arches. This is, of course, but the natural life history of every new discovery or invention in medicine, and the roentgen ray has certainly been no excep-

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tion. Many years have been required and much toil and perseverance have been necessary to determine and establish the real value of roentgen and radium therapy in the treatment of neoplastic diseases. This is now an established fact generally accepted by the medical profession and the laity. Unfortunately this fact is so firmly fixed in the mind of the layman that the use of radium and the roentgen rays has come to mean to him only one thing, namely, the presence of cancer. Nothing is farther from the truth, and it is becoming necessary to educate, not alone the laity, but physicians as well, that the day is rapidly approaching when the use of radiation for non-neoplastic conditions will equal if not surpass its use in the treatment of tumors.

And thus during the past decade there has been an ever increasing realization of the value of roentgen therapy in the treatment of inflammatory conditions, and it is, of course, in this category that this form of therapy for sinusitis finds justification. The writings of Manges, Desjardins and Hodges, to mention but a few of the outstanding contributors to this field, bear witness to the accumulating evidence that roentgen therapy is rapidly becoming recognized as one of the methods of choice in combating inflammatory lesions of all varieties. This fact has not yet completely permeated the medical profession, and many physicians remain in ignorance of this valuable adjunct to the therapy of inflammatory diseases.

It is but natural that one should ask for the rationale and the *modus operandi* in the treatment of inflammation by roentgen irradiation. The basis for this was recognized long before this form of therapy came into being. The research of Desjardins has brought to light a long list of experimenters and observers dating back as far as 1903 who have placed upon a firm foundation the mechanism whereby the physiological reaction known as inflammation is counteracted by the biological effects of roentgen rays. This action is based upon the well-established fact that there is a specific response to irradiation by every type of living cell. This specificity is well illustrated by the difference in response of the various cellular elements of the blood. Thus it is noted that the erythrocytes are quite resistant to irradiation, while the leucocytes are among the most sensitive cells of the body. And even among the various white cells there is a variation in sensitivity, the lymphocytes being much more readily affected than the polymorphonuclears. This was confirmed by research conducted by us a few years ago relative to the effects of therapeutic irradiation upon the blood as determined by the blood count. Patients receiving intensive irradiation, as for

malignant disease, invariably develop a leucopenia. Although all varieties of white cells take part in this leucopenia, nevertheless, the greatest reduction in numbers occurs in the lymphocytes. This unusual sensitivity of the lymphocytes to irradiation is taken advantage of in the roentgen treatment of such lymphatic disorders as Hodgkin's disease, lymphosarcoma and lymphatic leucemia.

The features common to all varieties of inflammation consist essentially of an active hyperemia, edema and a variable leucocytic infiltration with a preponderance of round cells. The intense congestion resulting from the increased circulation, the edema and the round cell infiltration is responsible for the swelling, heat, pain and tenderness which characterize the inflammatory reaction. The effect of irradiation upon such a process is the immediate disintegration of large numbers of leucocytes, especially the lymphocytes, which become engulfed by phagocytic cells and are removed from the site of inflammation. In this manner is the local pressure and thus the pain relieved by irradiation. It is also believed that with the destruction of the leucocytes there is the liberation of antibodies and ferments which aid in combating the cause of the inflammatory reaction.

These facts find ample confirmation in clinical observations. One of the best lesions for such observation is the furuncle which now is so frequently treated by roentgen therapy. If such a lesion is treated within 24 to 48 hours after its onset, that is at the height of the leucocytic infiltration, the process can usually be aborted and suppuration does not occur. If suppuration has started the treatment is less effective; the lesion cannot be aborted, but the process of suppuration is hastened. The pain is relieved, but relief is less rapid than in the early stage of the process. When suppuration is definitely established the only effect of irradiation is to hasten the time when the products of suppuration can be evacuated either spontaneously or surgically. After drainage has been established roentgen irradiation will shorten the course of the healing process. In the early stage of a furuncle, when the lesion is most responsive, the roentgen dosage applied must be relatively small. As the process becomes more chronic the dosage must be increased, and often a more deeply penetrating ray is required. It must be definitely understood that roentgen rays have no germicidal effect, bacteria being extremely radioresistant. The beneficial effect of irradiation is entirely the result of its influence upon the defensive mechanism of the body. Since this mechanism can very definitely be interfered with by too intensive irradiation it is extremely important that the

roentgen dosage be small and administered preferably in fractional doses. As shall be seen later, the factors as outlined above find their counterpart in the treatment of sinusitis by irradiation.

If one reviews the literature on the roentgen therapy of sinusitis it will be found that the results obtained by the various writers have been fairly uniform. There is some difference of opinion regarding the types of sinusitis to be treated, although this selection is rapidly becoming standardized. The greatest variation will be found in the technic employed, as will be subsequently discussed.

Osmond, in 1923, gave a preliminary report of 12 cases; 10 were treated in the acute purulent stage, three of them bordering on the chronic stage, and two were in the acute catarrhal stage. He used low voltage therapy, moderate filtration and a small dosage. Regarding his results he quite rightfully states that "it is too early to say that the application of the X-ray cured the sinusitis, but at least it seems fair to state that the application of the X-ray was coincident with the relief of the symptoms and the cessation of pus in all the cases." He felt that the X-ray offered a method of preventing the acute catarrhal condition from becoming purulent and the acute purulent sinusitis from becoming chronic. He was definitely of the opinion that no benefits could be expected from the treatment of chronic sinusitis especially when polypi had formed or necrosis of bone was present.

In 1932 Butler and Woolley reported their results in the treatment of 100 cases of chronic sinusitis considered by their physicians as unresponsive to other forms of therapy and therefore requiring operation. In this group as the result of roentgen therapy 31% of patients were rendered symptom-free, 50% definitely improved and 19% unchanged. This report aroused considerable interest and a certain amount of misgiving regarding the possible dangers of such treatment. Accordingly experimental work was done upon cats by Dr. Ralph Fenton, of the Department of Otolaryngology, and Dr. Olof Larsell, of the Department of Anatomy of the University of Oregon Medical School. These investigators produced acute frontal sinusitis in cats, some of which were subsequently treated by roentgen rays while others were used as controls. After the animals were sacrificed the tissues of the paranasal sinuses were studied grossly and microscopically. A summary of Dr. Larsell's findings is as follows: "The effect of the X-ray treatment appears to be due primarily to an early destruction of the lymphocytes in the infected membranes. About 48 to 72 hours after treatment of membranes which have been infected for several weeks, there appears to be an increase in

the number of macrophages. These are believed to come in response to substances released by the breaking down of the lymphocytes. These macrophages are seen to be laden with cellular debris and blood pigments. It is possible that they also engulf bacteria.

"The membrane becomes gradually reduced in thickness but retains numerous plasma cells, polymorphs, and some histiocytes. After a week or more some fibrosis appears. Several weeks after irradiation, nodule-like masses of lymphocytes may be seen in some of the membranes, indicating a return of lymphocyte formation.

"There is no evidence of injury to the cilia, epithelium, or cellular elements other than the lymphocytes as the result of X-ray dosage. The fibrosis is considered a result of the inflammatory process and the increased number of histiocytes immediately following the infection.

"In the animals given the double dose there was in one instance some indication of abnormal activity of the epithelium."

This investigative work is of the utmost importance as it not only establishes the rationale for roentgen therapy but shows that no permanent damage is done the tissues.

In 1934 Butler and Woolley presented a second report giving their clinical experience based upon a series of 700 cases. In this series they were able to obtain a satisfactory follow-up in 450 cases, which showed 36% entirely relieved, 55% definitely improved and 9% only slightly improved or not helped at all. The technic employed is as follows: "120 K.V.P., 5 ma., 11 inch distance, 4 mm. of aluminum filter, for ten minutes through a port one and one-quarter inch in diameter. These factors as applied by our equipment give a dose of 800 roentgens as measured with the Victoreen instrument with back-scattering. This dose is applied over each group of cells separately, but all involved areas are treated upon the same day. The central ray is so directed as to produce a cross-firing of the posterior ethmoid and sphenoid cells. The eyes and the nose are carefully protected at all times." This dosage amounts to approximately 500 roentgens as measured in air, which is the means used by most radiotherapists for measuring dosage.

Butler and Woolley call attention to the fact that failure of roentgen therapy does not interfere with subsequent surgery and emphasize the necessity for complete co-operation with the referring physician and the proper selection of cases.

In the latest article by Butler and Woolley (1938) they report that they have observed the clinical results of roentgen irradiation in chronic sinusitis in well over 2000 treatments during the past seven years. The type of cases treated and general results remain the same as in their previous reports. They continue with the single large dose technic repeating the treatment in six or eight weeks if indicated. They have more recently resorted to the use of deep therapy with equally good results. They conclude their article with the following statement: "From our experience with roentgen therapy in chronic sinusitis we are firmly convinced that it has a very definite place in the treatment of this widespread disease. In the hands of a skilled roentgenologist it is capable of accomplishing much good and is not harmful. It is worthy of wider consideration by rhinologists and radiologists than has heretofore been accorded it."

Rathbone (1937) directs attention to the value of roentgen therapy of chronic sinusitis in children. He emphasizes the fact that the symptoms of sinusitis in children are often slight or masked entirely by its sequelae and that to prevent the serious complications of later life the recognition and treatment of sinus disease is of the utmost importance. He calls attention to the frequent association of otitis media and mastoiditis with sinus infections and recommends that in repeated attacks of these conditions investigation of the sinuses should be done. He states that he has been able to terminate abruptly these attacks by treating an unrecognized sinus disease. The same holds true for asthma and cervical adenitis. The relationship of diseased adenoids, tonsils and diffuse lymphoid hyperplasia of the nose and throat to sinus infection is emphasized. The adenoids are readily seen in lateral films of the sinuses. The treatment of choice in these cases is the removal of the adenoids and tonsils, but when the patient is too young for these procedures, or in the presence of an active sinusitis roentgen therapy will often carry the patient along until operation can be done.

According to Rathbone the ideal patient for roentgen therapy is the child with a diffuse lymphoid hyperplasia throughout the nose and throat, with a watery or mucoid nasal discharge, a history of frequent colds, a chronic cough, and hyperplasia of the mucosa of the antra or ethmoids, as demonstrated by the roentgenogram. These cases are always helped and the result is permanent; they have fewer colds and the sinuses rarely become involved. If involved, they clear in a few days. The importance of including in the field of irradiation the adenoids and the lymphoid tissue of the throat is emphasized. The adenoids will usually regress 25 to 30% as the result of irradiation.

Rathbone treated 120 cases in three and a half years. A roentgen examination of the sinuses was made at the end of treatment and then every six months thereafter. It was possible to follow 70 of the cases treated, and these were classified as cured, improved and not improved. The cured cases had had immediate improvement after treatment, had remained symptom-free for one to three and one-half years, and the check-up roentgen examinations showed the sinuses to be entirely normal. The improved cases were those in which the local symptoms and sequelae were greatly or entirely relieved, but the check-up roentgen examination showed definite sinus disease to be present. Of the 70 cases there were 57% cured, 28% improved and 15% not improved.

It is of interest to note that in Rathbone's cases two somewhat opposing types of technic were employed. In one hospital, superficial therapy was used, while in a second, deep therapy was utilized with apparently equally good results. The factors for the superficial therapy were 125 K.V. (peak), 5 ma., 12 inch distance, 5 mm. aluminum filter, with a dose of 120 r. (measured in air). The deep therapy factors were 220 K.V. (peak), 20 ma., 50 cm. distance, 0.5 mm. copper filter, with a dose of 100 r. (measured in air). Three overlapping areas, 10 x 10 cm. or 7 x 7 cm., were used, one anterior and one right and left lateral. The anterior area extends from slightly below the hairline to the upper lip, while the lateral areas extend from the mastoid to the forehead, thus including the mastoids and the eustachian tubes. Six treatments were given, three times weekly for two weeks, one area per treatment, either 100 or 120 r. The eyelashes and brows were protected. In children with severe cough the chest was treated once or twice with 100 r. at conclusion of the sinus treatment. In seven cases the series was repeated at the end of six months or a year, with excellent results in four of them.

In collaboration with McLendon, Rathbone has published a more recent paper in which his series of cases of chronic sinusitis in children treated by irradiation has increased to 291. Uniformly satisfactory results have been maintained, and the general conclusions are essentially the same as in Rathbone's original paper. The more recent article is largely devoted to the pediatric aspects of sinus disease and again emphasizes the close relationship of otitis media, mastoiditis, tonsils, adenoids, lymphoid tissue of the upper respiratory tract and the lungs to the condition of the paranasal sinuses. The importance of the health of these structures to the general well-being of the child is stressed. According to these authors chronic sinusitis in childhood was not believed to exist until a few years ago. It is rather pointedly

inferred that the only way to prevent chronic sinusitis in adults is to cure sinusitis in childhood.

Hodges, who has given much attention and written many articles on the treatment of inflammatory conditions by irradiation, has had considerable experience in the treatment of sinusitis by this method. His results (1938) have been particularly gratifying. He stresses the important relationship between chronic sinus disease, often unsuspected, and chronic bronchitis and bronchiectasis, and believes that proper and early attention to the sinus pathology will prevent much of the chronic broncho-sinusitis of adult life. He does not treat acute sinusitis as a rule, believing that it can best be taken care of by the rhinologist. He stresses the value of antral washings. In the exceptional acute case given irradiation he insists upon free drainage of the purulent discharge, shrinkage of the nasal mucosa and small doses of roentgen rays. His best results have been obtained in those persistent cases of acute sinusitis that have been resistant to the ordinary methods of treatment; those cases with a chronic cough and recurrent colds in which sinus disease may or may not be evident clinically; and the chronic hyperplastic sinusitis with early polyp formation of not too long standing. It is of interest to note that in those patients showing an increase in the bronchovascular markings in the bases of the lungs, in addition to sinus disease, Hodges applies small doses of roentgen rays to the bases of the lungs and thus obtains much quicker results. Hodges recognizes the importance of allergy in the sinus problem and advises that this aspect of the case receive attention.

The technic employed is as follows: 130 K.V. peak, 6 mm. aluminum filter, 25 cm. skin target distance. About 100 to 300 r. measured in air, the dose dependent on the type of case, is given in three or four treatments in from ten days to two weeks. The single large dose has been used in some cases, but a few fairly severe reactions seem to favor the above technic. Small doses are always used in children.

In a more recent article by Hodges and Snead (1939) there is reiteration of the essential features of the original paper with the important statement that the authors "are more enthusiastic than ever before over the results that can be obtained by irradiation in the treatment of certain types of infections of the nasal accessory sinuses."

The report by Warren (1935) is of particular interest. Although aware that best results from irradiation therapy are obtained in selected cases of sinusitis, he purposely avoided selection, treating 72 cases of all types. Furthermore, during and after the X-ray treatment no other form of treatment was given in 80% of the cases,

so the results would not be confusing. He treated all types except the atrophic, including the hyperplastic, the purulent, cases with polyposis and cysts, asthma due to sinusitis, iritis with focal symptoms in the sinuses, and allergic nasal manifestations, and gave X-ray therapy following submucous resections. His results showed 25% with marked improvement, 40% with moderate improvement, 20% with transitory moderate improvement and 15% with no improvement. No case had been followed for more than two years. He found definite improvement in some of the conditions commonly associated with sinusitis, such as rheumatism, bronchitis, asthma, bronchiectasis, iritis and allergic rhinitis.

The technic employed consisted of 80 to 90% of an erythema dose, with 150 K.V.P., 25 ma., 3 mm. aluminum filter, 50 cm. distance, 6 minutes to each area. Each sinus was treated individually with cross-firing on the sphenoids. Overlapping of areas was avoided and the tip of the nose protected to avoid subsequent dryness of the nasal mucosa. The patients were warned of the symptoms of an acute cold following treatment, but many showed no such reaction.

Smith and Nickel (1938) report their experience in the treatment of 25 cases of subacute and chronic sinusitis observed from four months to a year. All had sinus headache and more or less nasal discharge. The best results (100%) were obtained in that group in which the appearance of the nasal mucosa was that of an acute stage of vasomotor rhinitis. Their technic consisted of 135 K.V. (peak), 5 ma., 4 mm. aluminum filter, 12 to 14 inch distance with the use of a cone; 150 to 200 r. (400 r. = erythema) were given at two to three week intervals for three to five treatments. Congestive symptoms usually followed such treatments. Cases of acute sinusitis requiring surgery should not be treated, they concluded.

Dysart (1939) presents a report on X-ray treatment of infections with a review of the literature and a report of cases of mastoiditis and sinusitis. His interest in this subject came about as the result of an observation made about five years before in which a decided clinical improvement was noted in a number of cases of acute mastoiditis following the taking of X-ray pictures for diagnosis. He relates some interesting experiences in this respect and tells of a most unique case reported by Watkins, from which he quotes as follows: "The writer's attention was first called to the beneficial effect of roentgen irradiation in sinusitis by a rhinologist who suffered from a chronic infection of the nasal accessory sinuses. He came at fre-

quent intervals to have a complete set of sinus pictures made, and finally volunteered the information that he had the pictures taken for their therapeutic effect. He found from experience that the amount of exposure required to make six films, necessary for adequate examination, was just the amount of radiation he needed for relief of symptoms for about two months. He stated that he had long since learned never to explore the antrum until X-ray treatment had been tried and failed, and he seldom found it necessary to invade the antrum either through the natural or artificial opening."

Dysart reports several cases of mastoiditis and sinusitis treated by irradiation with good results.

Firor and Waters (1939) have given an excellent review of the subject. They have obtained microphotographs to show the variety of cellular pathology that occurs in the various types of sinusitis treated by roentgen therapy. This helps considerably to understand the reason for the beneficial effects in certain cases and not in others. They conclude from their own experience that approximately 70% of properly selected cases of sinusitis can be cured or markedly improved by irradiation. The technic employed by them is 125 K.V., 5 ma., 35 cm. focal skin distance and with filtration of 4 mm. aluminum. They give four semi-weekly doses of 100 r. each, measured in air. At times it has been necessary to use 600 r. over a three-week period to obtain the maximum desirable result.

Dell has had considerable experience in the treatment of sinusitis in children. His technic and results are very similar to those reported by Rathbone. He also emphasizes the value of the lateral film for the detection of adenoids and considers allergy one of the most important factors to be investigated in each case. He states, "I am definitely convinced that X-ray treatment of sinus disease in infants and children is almost a specific, but I do believe that it is very important to establish the diagnosis of chronic sinus disease and not treat the acute ones, as a majority of these clear without treatment. I have seen what to me are almost dramatic results in cases of marked malnutrition in children with sinus disease, manifested by rapid gain in weight and vigor."

Gatewood (1940) asks the question, "Of what value is roentgen therapy for sinusitis?" and gives a rhinologic study of 22 cases. This paper is refreshing, as it must be admitted that the review of article after article with nothing but enthusiasm does become monotonous. Gatewood's chief objection to previous reports is that they

have been made almost entirely by radiologists, and therefore the accuracy of the results cannot be accepted. How he arrives at the conclusion that previously reported cases did not have rhinological verification of diagnoses and results he does not state. Most writers have specifically emphasized the necessity of complete cooperation between rhinologist and radiologist.

Gatewood's examination of these 22 cases consisted of the taking of histories, clinical inspection, investigation by shrinkage, suction and lavage and comparison of films taken before and after treatments. We must assume that this method was not employed by other investigators. He does not state whether any selection of cases was made, and the technic employed for the roentgen therapy is not given. Of the 22 patients studied, four showed complete relief of symptoms. The clinical findings were entirely normal and the diagnostic films clear. He states that these patients were considered, in a sense, well. Eight patients were symptomatically improved. Ten patients thought that they were not helped symptomatically. Four of the ten patients who did not show clinical or roentgen change in their condition after treatment were operated upon. Gatewood agrees that irradiation does not make operation more difficult or interfere in any way with the healing or end result. Microscopic study was made of the tissues removed at operation in these four cases, and the results confirm the findings of others. It could not be shown that any damage had been done the tissues by the irradiation. It is well known, of course, that the small amounts of irradiation used in the treatment of sinusitis do not produce any permanent changes in the tissues. These effects can be found only if the tissues are studied within a few days to a week after radiation. This fact was confirmed by Gatewood who found changes in one patient operated on six days after treatment.

A recent article by Williams and Popp (1940), a rhinologist and roentgenologist working together, is an attempt to answer Gatewood's objection that the fact that most of the literature on the subject of the treatment of sinusitis with roentgen rays has been produced by radiologists alone makes it difficult to evaluate the end results reported. Aside from this fact, this paper is of particular importance since these investigators treated acute sinusitis, the type of sinusitis which most previous writers on the subject have especially avoided.

Williams and Popp accepted for roentgen treatment only cases of acute sinusitis in which pain and tenderness were the principal

symptoms. They divided their cases on clinical grounds into two groups, moderate and severe types, and these were further divided into those patients in whom symptoms had been present for one to five days before treatment was instituted and those in whom symptoms had been present for more than five days. This was done in order to prove or disprove the statements in the literature that treatment is more effective early in the course of an inflammation. The criteria used to indicate good results in this investigation were the disappearance of pain within one to six hours after the roentgen treatment, disappearance of tenderness within the same interval of time, disappearance of congestion from the nasal mucosa and cessation of discharge into the nasal chambers from the sinuses. The majority of the patients received additional treatment by the Dowling pack method, although in many cases relief by this method had failed to ensue before roentgen therapy was instituted. Some patients received hot compresses and sulfonamide drugs as well. Fifty-six patients were treated, 31 with severe involvement and 25 with moderately severe. The method of treatment consisted of the use of 130 K.V. (constant potential), filtered through 6 mm. of aluminum except in children, for whom a filtration of 4 mm. of aluminum was used at a distance of 40 cm. Only those sinuses giving symptoms and showing objective evidence of involvement were treated. The doses used in each case were in accordance with the duration and severity of the infection. Fifty roentgens were used in patients with symptoms of from one to five days' duration and 75 to 100 r. in those with symptoms of more than five days' duration. For each patient, treatments were repeated on alternate days, from one to three treatments being given, depending on the symptomatic response.

The authors give a detailed report of the results obtained in each of the four groups of cases. Their clinical impression is as follows: "The most striking effect of roentgen therapy of acute sinusitis is the relief of pain and headache. Such relief is noted early in cases in which there are favorable results from this type of therapy. This relief of pain is often accompanied by a noticeable increase in the discharge, so that the effect of roentgen therapy on the sinuses may be due to diminishing the engorgement of the nasal mucosa. This effect is definitely observable. If no other effect were obtained, symptomatic relief is great enough to justify the use of this therapeutic method. More good results seemed to be obtainable when therapy was instituted early, and the results seemed to be better in an initial attack of sinusitis than in recurrence after one or more previous attacks. Although not implicit in material presented,

there seemed to be an effect of preventing recurrence of infection in cases in which patients had previously been subject to repeated recurrence of attacks of acute sinusitis. While roentgen therapy can by no means be depended on as the sole therapeutic agent in cases of acute sinusitis, it would seem to form a very useful adjunct method of therapy, especially in regard to symptomatic relief. It is suggested by this study that the severity of the symptoms and the duration of the disease are inverse to the therapeutic results obtainable."

COMMENT

An attempt to evaluate and interpret the results of roentgen therapy of sinusitis, as reported in the literature as well as from my own personal experience, leads to certain rather definite conclusions. While I have made no attempt to follow the cases that I have treated and have no statistical data to offer, my experience in this field covers a period of ten years and some four to five hundred cases. In general my experience coincides very closely with those that have been reported by other observers.

In the first place it must be recognized that an attempt to evaluate any form of therapy for sinusitis is very difficult. The extreme variability of this disease, its tendency to spontaneous remissions, the individual response to infections in general, the complications imposed by allergy and the marked variation in the anatomical make-up of the sinuses introduce factors all of which must enter into the problem of any individual case of sinusitis. Under these conditions the fact that most investigators have obtained approximately the same results seems rather remarkable but tends to substantiate the accuracy of the individual reports. Sufficient experience has now accumulated that the roentgen therapy of sinusitis can no longer be regarded as experimental.

Certain facts have been stressed by most observers. First and foremost is the absolute necessity of team-work between the rhinologist and the radiologist. Certainly the roentgenologist alone cannot cope with this problem. While the roentgen examination is extremely important in obtaining information of the actual condition of the sinuses, this is but a part of the general investigation of the patient. The rhinologist's local examination of the nose and sinuses and his general survey of the patient and interpretation of the history are of primary importance. Often the aid of the internist or pediatrician, who should give due consideration to the question of allergy, must be sought. The medical profession is gradually coming

to the realization that the practice of medicine is becoming more and more a matter of cooperation between various groups of specialists all lending their special talents to the solution of a given problem. Nowhere is this better illustrated than in the subject at hand.

The proper selection of cases of sinusitis for roentgen therapy cannot be too strongly emphasized. This selection must be made by the rhinologist. Failure to observe this general rule is certain to bring the method into disrepute and no doubt accounts for some of the adverse criticism that has already occurred. It would be well to summarize briefly the prevailing opinions regarding the use of roentgen therapy in the various forms of sinusitis.

Acute sinusitis: Most observers believe that acutely inflamed sinuses should not, as a rule, be subjected to irradiation. The reason given for this is the fact that acute infections of the sinuses show a marked tendency to spontaneous cure, or respond readily to local treatment. There is always the fear that irradiation may aggravate an acute sinusitis by temporarily increasing the local congestion or by blocking the ostia of the sinuses and thus prevent drainage. Thus Hodges insists upon free drainage and the shrinkage of the nasal mucosa before resorting to roentgen therapy in acute cases. The fact that these cases can be successfully treated is well illustrated by the experience of Williams and Popp. The problem here is quite comparable to the early stage of a furuncle when marked congestion and leucocytic infiltration are the predominant pathology. I have no hesitancy in treating this group of cases provided they are under the closest observation of a competent rhinologist. In these acute cases the dosage should never exceed 50 r. This is increased in subsequent treatments with regression of the symptoms. No predetermined amount of therapy is given, the treatments being administered as seems indicated by the rhinologist. An aggravation of symptoms, especially of pain or headache, is an indication that the dosage is too great. This should be further reduced in subsequent treatments or the method abandoned entirely. As a rule these patients obtain prompt relief of their symptoms, and usually one or two treatments given at 48 hour intervals suffice to initiate the process of recovery.

Subacute sinusitis: These are the cases in which symptoms persist for weeks and months after an acute attack and which do not respond to the usual forms of therapy. These patients complain of nasal blockage, stuffiness in the head, persistent nasal discharge, occasional headache but no pain. In the roentgenogram there will be noted a swelling or bogginess of the mucosa of one or more of the

sinuses, particularly the antra. This tissue is rich in leucocytic cells and therefore forms the ideal case for irradiation. This is the group that has received most attention by radiologists and accounts for the largest percentage of good results. These cases can be treated with moderate doses, that is between 100 and 150 r., and while many will respond to one or two treatments, I prefer to give them a complete series in order to secure as complete resolution of the process as possible and to prevent an early recurrence and chronicity.

Chronic hyperplastic sinusitis with exacerbations: Sufferers from this disease constitute a very large group who have, each winter, recurrent attacks of head colds of two or three weeks' duration. The attacks are initiated on the slightest provocation, are longer in duration than the average acute sinusitis, become increasingly more difficult to combat with the passing years, and are often accompanied by early pulmonary complications such as bronchitis or beginning bronchiectasis. Roentgenograms show persistent but variable degrees of clouding of one or more sinuses due to hyperplastic mucous membrane. This membrane is the site of an infiltration of leucocytes but one considerably less marked than in the subacute cases. There is a variable amount of fibrosis present. In general this disease shows a fairly satisfactory response to roentgen therapy. The results will be in direct relation to the amount of leucocytic infiltration as compared to the fibrosis of the sinus mucosa. These cases should receive full courses of roentgen irradiation with maximum dosage. It may be advisable to repeat the series of treatments once or twice in subsequent years.

Chronic sinusitis with extensive fibrosis: In this group also belong the patients who have had repeated operations for sinusitis but who continue to have trouble. These patients are never free of symptoms regardless of the time of year; they are sinus-conscious, usually in poor general health and often have a superimposed neurosis. The roentgenograms usually show a pan-sinusitis with dense clouding and complete lack of aeration of the sinuses, often with a dense reactive osteitis. My experience in this group has been the same as others who have treated these unfortunate patients. They seldom respond to roentgen therapy since there is no leucocytic infiltration to be affected, and the dense fibrous tissue present is highly radioresistant. These cases are readily recognized both clinically and roentgenologically. These are the patients for whom surgery gives such notoriously bad results, and yet they are operated upon time and again. One unfortunate physician had had 23 operations upon his sinuses, and when I saw him, was entering the hospital for his 24th. The

statistics of roentgen therapy would be materially improved by refusing to treat this type of case, but occasionally one sees a brilliant symptomatic improvement in the absence of any demonstrable clinical or roentgenological effect. For this reason these patients should not be denied any possible benefit that irradiation may hold for them, particularly if operation can thus be avoided. These patients should have a full course of irradiation, preferably with deep therapy and with the maximum dosage. The treatments should not be repeated unless there has been definite improvement from the first series. Repeated exposures to the roentgen ray will tend only to increase the fibrosis already present.

Sinusitis with polypi and cysts: The irradiation treatment of sinusitis is not influenced by the presence of polypi or cysts. If these lesions are composed of a sensitive type of tissue they will respond to irradiation. When true fibrous polypi are present no result can be expected from roentgen therapy. Such lesions are not radiosensitive, and I have never felt that the large amount of roentgen irradiation required to affect them is justifiable in view of possible late effects that may occur in the skin. The use of radium locally is, of course, another matter. A number of investigators have reported good results in the use of roentgen therapy following the surgical removal of polypi, in order to prevent recurrence. This is worthy of trial, but such treatment should be kept well in the bounds of safety.

Atrophic sinusitis: I have always considered roentgen therapy distinctly contraindicated in this type of sinus disease. Certainly the tendency of irradiation is to dry up secretions and dehydrate tissues. Since these are the features of an atrophic sinusitis, no form of therapy which produces these effects seems indicated. I have never been sufficiently convinced of the stimulating effect of irradiation to advise its use for this purpose, and I doubt very much whether the tissues of an atrophic sinusitis are capable of stimulation.

Sinusitis with asthma: The roentgen treatment of sinusitis should not be materially influenced by the presence of asthma. It is important to recognize that the sinusitis may be the result of the asthma or vice versa. Every chronic sinus victim should be studied from the standpoint of allergy. Obviously no form of therapy for sinus disease will be effective unless the presence of allergy is recognized and successfully combated. Vasomotor rhinitis on an allergic basis has, in my experience, shown very satisfactory symptomatic response to roentgen therapy. As has been noted, the results of different observers in the treatment of this group of cases has been

quite variable. An attack on the sinus aspect of such cases alone will be of little avail; the problem is a much larger one.

Sinusitis in children: This is by far the most important group to be considered. I am convinced that the only hope of combating many of the chronic ailments of the respiratory tract in adults is the prevention of chronic sinusitis in childhood. Most, if not all, of the chronic incurable conditions of adults such as chronic sinusitis, bronchosinusitis, bronchiectasis and chronic pulmonary emphysema, are merely the terminal events of a neglected sinusitis in childhood. The close relationship of diseases of the sinuses and the lungs is not sufficiently appreciated by the medical profession. It has been seen from the various reviews that sinusitis in children is the most suitable form for roentgen therapy. Seldom does one encounter in childhood the chronic fibrous sinusitis that is not amenable to irradiation. Children are ideal patients for this form of therapy. There are no painful experiences, and cooperation of the patient is quite readily obtained. This is in sharp contrast to the difficulty of administering local treatment to these young patients. The adenoids and the hyperplastic lymphoid tissue of the nose and throat should also be irradiated along with the sinuses.

TECHNIQUE

The technic employed by each investigator was purposely included in each review. It is seen that hardly any two radiotherapists apply irradiation in the same manner for sinusitis, and yet the results are approximately the same. Gatewood took exception to this lack of standardization, and yet there appears to be no reason why a greater degree of standardization should exist in roentgen therapy than in any other form of treatment for sinusitis. As long as certain general principles of roentgen therapy are observed, the precise method of administration seems to be of no great moment. Since we are dealing with such sensitive tissues only small amounts of irradiation are required to be effective, and this is the principle that has guided most workers in this field.

Whether low or high voltage therapy is used makes little difference. Personally I have always had a preference for deep therapy, that is 200 K.V., except in children. The technic that I have most commonly employed is as follows: 200 K.V. peak, 30 ma., 0.5 mm. copper and 1 mm. aluminum filtration and 50 cm. skin target distance. Three portals are used, an anterior and a right and left lateral. These are large enough to include all the sinuses. The pa-

tient is treated three times weekly, one area at each visit. Starting with the anterior area, each portal receives 100 r., as measured in air, until each area has been treated twice. Two additional treatments are given to the anterior portal. Thus the patient receives eight treatments with 400 r. total to the anterior and 200 r. to each lateral portal. The greatest amount of treatment is given to the anterior area because it is felt that this is the closest and most direct approach to all the sinuses. Occasionally the lateral portals are omitted entirely, and not infrequently only a part of the total treatment is given. Only seldom have I treated individual sinuses as advocated by some workers. I have rather felt that sinusitis is usually a diffuse disease involving all the sinuses to a greater or less extent and that the patient's best interest was being served by treating all the sinuses. A normal sinus will not be affected by the amount of irradiation given. It is important that one should make his technic as flexible as possible so that it can be varied to suit the needs of the individual patient. Individualization must be practiced here, as in treating other conditions. In acute sinusitis the dosage is smaller, not exceeding 50 r., and no set number of treatments is given, therapy being stopped when considered advisable by the attending rhinologist. In the acute cases I may use superficial or deep therapy as the needs of the patient seem to indicate.

I have in recent years used a modification of our usual technic, which has given very encouraging results in all cases in which it has been employed. In this modification only the large anterior portal is used. The physical factors remain the same. The patient is given 100 r. once each week for four weeks and then one treatment every two weeks for four additional treatments. Thus eight treatments totaling 800 r. are given over a period of three months. This will carry the patient over the worst part of the winter and will relieve him of the three or four attacks of sinusitis that he has customarily had each winter. Further experience with this technic will be required to determine whether the encouraging results so far obtained can be continued. In children superficial therapy is employed using 130 K.V. peak, 5 ma., 4 mm. aluminum filtration, 30 cm. skin target distance using either one or three large portals including all the sinuses, 75 to 100 r. being given every other day for from four to six treatments. In all cases the eyebrows, eyelashes, and hair are protected by lead shields. In adult males the upper lip is also protected as one rather susceptible blonde found it unnecessary to shave his upper lip for about three weeks following a series of treatments of the usual dosage.

Reactions: In properly selected cases and with proper technic there should be no unfavorable reactions. If pain is present this is usually relieved within a few hours after the treatment. If pain results from the treatment the dosage has been too great. With the larger dosages there may be some evidence of nasal congestion several hours following treatment. This has usually disappeared by the following day. Many patients have an increase of nasal discharge following each treatment. In patients that are going to be benefited, symptomatic relief follows the first treatment as a rule.

In the hands of competent radiotherapists there are no harmful effects. It is necessary to protect the eyebrows, eyelashes and hair because in susceptible individuals epilation may occur. This may be distressing to the patient, but he can be assured that the loss of hair will not be permanent. There is not the slightest danger to any of the neighboring tissues that may receive stray radiation. The eyes, nerves and brain are exceedingly resistant to irradiation. Most normal structures are not easily influenced by roentgen irradiation, and this is true of the hypophysis which is often mentioned as a possible source of danger in sinus irradiations.

Results: The evidence already deduced from the articles reviewed is ample proof of the benefits to be derived from this form of therapy. In acute cases one can expect definite relief of symptoms in the majority of cases with a shortening of the course of the attack. In the subacute cases one can expect prompt termination of the process, even when all other methods have failed. Chronic sinusitis of any variety is probably never cured regardless of the type of therapy used. These cases are, however, in many instances, definitely benefited by roentgen therapy. Certainly this method of treatment should be tried before resorting to surgery in chronic sinusitis, and in many instances surgery becomes unnecessary. I do not believe that irradiation or any other form of treatment will cure sinusitis if one means thereby that the patient will never have another attack. My experience indicates, however, that patients are rendered less susceptible to recurrences for months and years following a full course of irradiation therapy. The enthusiasm of most patients who have received this form of treatment speaks for itself.

My first experience with this form of therapy some ten years ago left me so enthusiastic that I felt that the solution to the sinus problem had been found. I am definitely less enthusiastic at the present time. I have come, however, to a sounder appreciation of its real value and its limitations. Roentgen therapy for sinusitis is

not a panacea. Anyone who uses it with this idea is doomed to disillusionment. This is something that must be tried for oneself and its value must be determined on the basis of one's own personal experience. Anyone who uses roentgen therapy for sinusitis with an open mind, in properly selected cases, with proper roentgen technic, and under proper clinical supervision is certain to be convinced of its effectiveness and value as an adjunct to our present therapeusis of sinusitis.

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Clinical Notes

XL

HEMORRHAGIC CYSTS OF THE FRONTAL SINUS WHICH SIMULATED MUCOCELE: REPORT OF TWO CASES*

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Two patients were encountered whose symptoms and signs were thought to be due to mucocele of the frontal sinus, but exploratory operation revealed that hemorrhagic cysts of the frontal sinus had caused the symptoms and signs. Because this type of cyst is rare and because the operative technic employed in removal of the cysts differed from that used in the management of mucocele of the frontal sinus, the cases are reported in detail.

The literature is replete with reports of conditions which affect the frontal sinus, including infections, mucoceles and osteomas. Cysts of the frontal sinus are reported infrequently. Perusal of the literature disclosed that papers dealing with cysts of the frontal sinus usually consisted of reports of a single case. The majority of these cysts were described as cholesteatomas. Of the reports reviewed, no mention was found of hemorrhagic cysts of the frontal sinus.

An early reference to cholesteatoma of the right frontal sinus is found in a report by Haeggström[1] in 1916. Hayden,[2] in 1925, mentioned a case of what he believed to be true cholesteatoma of the frontal sinus, although it was found to be present several years after a Killian operation had been performed. One of us (Lillie[3]) reported a somewhat similar case in which cholesterol crystals and cheesy matter were found in the sinus. Oberronder,[4] in 1929, reported the case of cyst of the left ethmoid and frontal region which invaded both frontal sinuses. Microscopic examination of the tissue removed at operation revealed extensive hemorrhage and localized

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infiltration with round and plasma cells, the plasma cells predominating. Included in the membrane were cholesterol spaces bordered by giant cells. From his study, Oberronder concluded that he was dealing with a cyst of syphilitic type which had originated in the labyrinth of the left ethmoid and had spread into the frontal sinuses and finally into the left orbit.

In 1930, Snell[5] reported the case of a large cyst, which had many interesting aspects. The cyst was larger than the patient's head and was thought to have its origin in the right frontal sinus. The contents of the cyst were described as "a quantity of sediment which was dark brown in color and contained a great many fine shining particles." There is no statement as to the structure of the particles in the original article. However, in a later publication dealing with the results of the microscopic examination of the tissue removed by Snell,[5] Kegel[6] reported that cholesterol crystals were present in the fluid removed from the cyst. Kegel concluded that the cyst was a mucocele of the frontal sinus. It is possible that the cyst, except for its size, was similar to those in the cases to be reported by us.

Spencer,[7] in 1930, reported in detail a case of cholesteatoma approximately 7 by 5 cm. in size, which was removed from the right frontal sinus and the roof of the orbit at operation. The report is interesting not only because of the rarity of the condition described but because of the apparent duration of the condition and the final outcome. At the age of 20 years, the patient was struck about the right eye with a piece of steel, after which a gradual increase in the prominence of the eye seemed evident. Twenty-three years later the cholesteatoma was found at operation. The patient died 11 years after this operation or a total of 34 years after the injury. Study of tissue removed by curettement from the interior of the right frontal sinus revealed "masses of epithelial cells of the squamous type growing atypically with the formation of horny pearls." It was concluded that the lesion was a squamous cell carcinoma of the orbit and frontal sinus. The types of formation of cholesteatoma (true cholesteatoma and false cholesteatoma) and their characteristics have been reviewed by Spencer.[7]

The recent report by Coates[8] include a reference[9] to a report of a case of cholesteatoma of the frontal sinus in which trauma was implied to have been the causative factor. Two cases are reported in detail in Coates' article. One patient had an infected cholesteatoma of the left frontal sinus and the second patient, observed by Woodward,[10] had involvement of the right frontal sinus. In this

case, cholesterol crystals, a cholesteatoma 2 by 3 cm. and pus were present at operation. Coates discussed in detail the differential diagnosis and possible etiologic factors of such lesions.

It is interesting to note the side involved in the cases reported; four were on the right, one on the left, one apparently originated on the left and involved both sinuses and in two instances no mention was made of the side involved.

Trauma in the region of the affected sinus is mentioned in the reports of Hartley,[9] Spencer and Coates.

REPORT OF CASES

CASE 1.—A laborer, 32 years of age, registered at the Mayo Clinic March 16, 1940, complaining of pain over the left frontal sinus, bulging of the left eyeball and drooping of the upper lid of the left eye. A year before admission he felt that there was a foreign body in the left eye, but none was found on examination. Drooping of the upper eyelid and bulging of the eyeball had been noticed for about four weeks prior to registration. No history of discharge from the nose or of symptoms of sinusitis was obtained. The patient remembered that when he was a boy he had been kicked in the forehead by a horse, although he could not remember on which side. A year previous to examination he had experienced severe pain in the outer aspect of the left frontal sinus which had lasted approximately an hour. No disturbance of vision had been noticed.

Examination revealed 14 14 vision in both eyes. Extraocular movements were normal in all meridians; visual fields were roughly normal and tactile tension appeared normal. Readings with the exophthalmometer set at 106 mm. were 19 mm. on the right and 21 mm. on the left. On examination the fundi were normal; the ears, nose and throat were also normal except that a mass was seen in the upper outer aspect of the left orbit. On palpation the mass felt like a rubber ball. Closer examination revealed a defect in the floor of the frontal sinus through which the mass presented. Proptosis of the eyeball was caused by the mass in the orbit. Roentgenographic examination of the left frontal sinus revealed what appeared to be a separate left frontal sinus in the outer aspect of the forehead (Fig. 1a). Closer inspection revealed that apparently a separate nasofrontal duct led from the nose to this part of the frontal sinus. These conditions were regarded as anomalous. The density of this region was increased but not sufficiently to be of diagnostic significance. The defect in the floor of the outer aspect of the frontal

a. *b.*

Fig. 1 (Case 1). Sinuses before operation. *a.* Postero-anterior view; the large cavity overlying the left orbital space and the absence of the bony orbital roof may be noted; there is no corresponding supra-orbital cavity on the opposite side; *b*, lateral view. Evidence of chronic suppurative sinusitis was not noted at any time.

sinus was not disclosed by the roentgenogram. A lateral roentgenogram (Fig. 1b) revealed a fan-shaped lesion with definite outlines and of different density from the surrounding bone under the zygoma. This change in the bone was attributed to some resorption of the bone, probably caused by pressure or lateral extension of a large frontal sinus. A tentative diagnosis of mucocele of the left frontal sinus with extension into the orbit was made and an external operation on the left frontal sinus was performed. A cyst of peculiar appearance was found in the frontal sinus. The wall was extremely thin and was dissected away from the periorbita and walls of the sinus with difficulty. Only the lateral aspect of the sinus was involved. The cyst contained a dark-green fluid and an amorphous mass of putty-like débris, suggestive of cholesteatoma. Bleeding from several blood vessels occurred when the wall of the cyst was removed from the posterior wall of the sinus. This apparently was the site of origin. At completion of the operation, the cavity was swabbed with tincture of metaphen and packed with a gauze strip which had been impregnated with petrolatum. No opening was made into the nose. The wound was dressed through the site of incision.

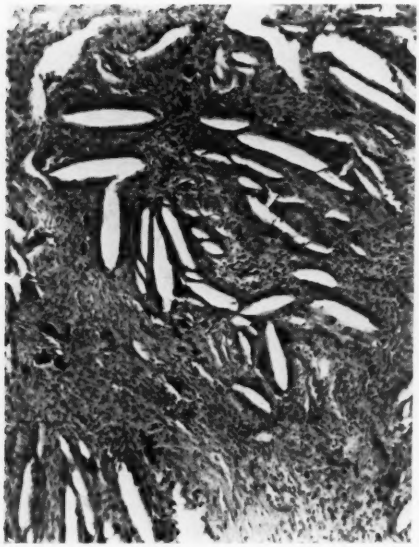

Fig. 2 (Case 1). Tissue from cyst of left frontal sinus; numerous cholesterol crystal clefts and small deposits of calcium may be seen (X72).

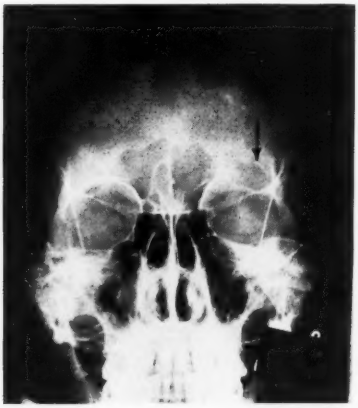

Fig. 3 (Case 1). Six months after operation.

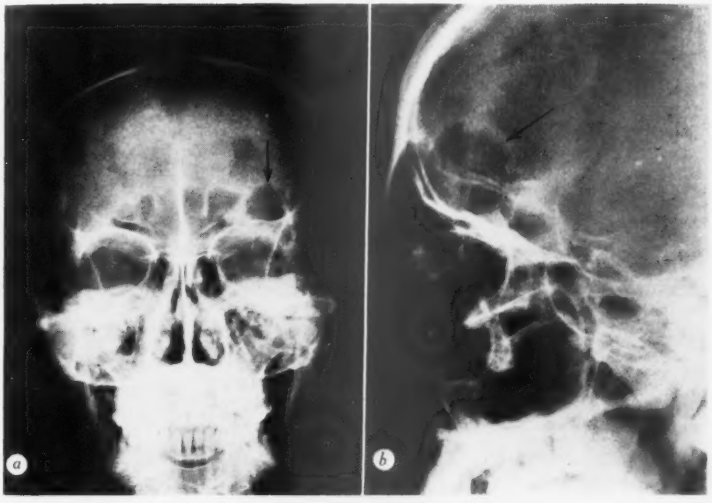

Fig. 4 (Case 2). Sinuses before operation. *a*. Postero-anterior view; well-outlined supra-orbital cavity on the right may be noted; *b*, right lateral view; the site of the cyst of the supra-orbital frontal sinus is outlined readily.

Convalescence was uneventful, except that ecchymosis of the eyelid and conjunctiva developed. Examination of the tissue removed at operation disclosed numerous cholesterol clefts and small deposits of calcium (Fig. 2). The patient was dismissed from the hospital on the sixth postoperative day and from the clinic three weeks later. He was examined four and eight months later and found to be in good condition (Fig. 3). Anesthesia or paresthesia of the forehead was the only symptom he had noticed.

CASE 2.—A steel worker, 42 years of age, registered at the Mayo Clinic on May 2, 1940, complaining of defective vision and bulging of the right eye of one year's duration. No history suggestive of sinusitis was obtained. The patient could not remember that he had ever been injured. For a number of years he had had episodes of severe pain over the right frontal region, which had lasted from one to three days. The episodes had occurred at intervals of three to six months. For a year, during which bulging of the eye had been noticed, the pain had not recurred.

Examination disclosed that the right eye was definitely proptosed outward and downward. Defects in the floor and outer table

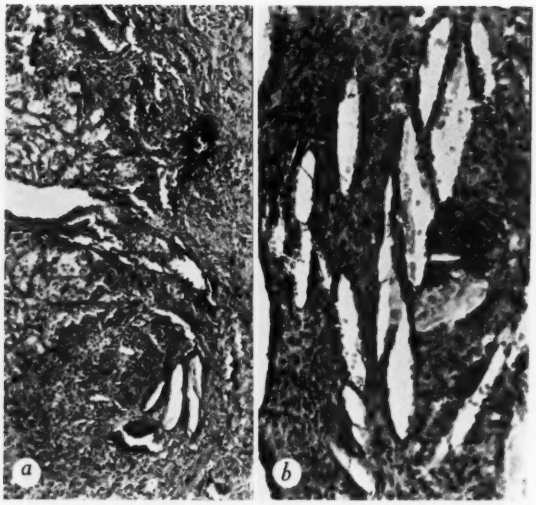

Fig. 5 (Case 2). Tissue from cyst of the right frontal sinus. *a*. Several cholesterol crystal clefts; the dark, stained structures are deposits of calcium; many foam cells may be seen (X72). *b*. Multiple cholesterol crystal clefts, one large deposit of calcium and much hemosiderin (X140).

of the frontal sinus could be felt on palpation. Extraocular movements were normal. Vision was 4/60 for the right eye and 6/6 for the left eye; the pupillary reflexes were normal. The visual views were roughly normal. Examination disclosed that the fundus of the left eye was normal, but in examination of the right fundus the disk and macular regions were elevated three diopters as compared to the rest of the retina. The posterior and central portions of the globe seemed to be pushed forward. Examination of the nose did not reveal evidence of sinusitis. Roentgenograms of the sinuses revealed that from the front the right frontal sinus apparently was divided into two parts (Fig. 4a); laterally, a ball-shaped defect of less density with definite outlines, located under the zygoma, was seen (Fig. 4b). There was no obvious pathologic change in the right frontal sinus. The defects in the floor and outer table of the frontal sinus could not be seen in the roentgenogram. A tentative diagnosis of mucocele of the frontal sinus which presented through the floor into the orbit and externally through the outer table was made.

An external exploratory operation was performed. The outer table of the frontal sinus was thin; many small defects were seen

through which a fluctuant mass bulged under pressure. The bone appeared dark. The mass was opened and much yellow fluid escaped. A large cavity was seen which was nearly filled with an amorphous putty-like mass of débris. The wall of the cyst was dissected away from the bone and periorbita with difficulty. The cavity extended down to the cone of the orbit, mesially over the globe into the ethmoid cells and externally under the anterior attachment of the zygoma. The point of origin of the cyst could not be determined with any degree of certainty. The wound was cleaned, swabbed with tincture of metaphen and packed with gauze impregnated with petrolatum. It was decided that the postoperative dressings should be done through the external wound rather than through an opening into the nose. The pathologist's report on the tissue removed from the right frontal sinus was inflammatory tissue containing cholesterol crystals and deposits of calcium (Figs. 5a and 5b).

Convalescence was uneventful, and the patient was dismissed on the 18th postoperative day. Subsequent reports from the patient reveal that his vision has improved greatly. However, the eyes have not been examined.

COMMENT AND CONCLUSIONS

Review of the salient features in these cases does not reveal a probable etiologic factor. The history of trauma as an etiologic factor in these cases is not definite enough to be given serious consideration.

The symptoms and signs for which the patients sought relief were of one year's duration. The first patient complained of dull pain; the second patient had not experienced pain since bulging of the eyeball had occurred. The first patient had one episode of severe pain which had lasted several hours; the second patient had similar episodes which had recurred at intervals over a period of years. This particular feature may be of great importance or significance from a diagnostic standpoint. It is possible that the pain was caused by hemorrhage into the cyst. The amorphous mass of débris, which on microscopic examination disclosed cholesterol crystals, suggests the probability of hemorrhage. The green fluid in the cyst of the first patient may have resulted from a more recent hemorrhage than the yellow fluid found in the cyst of the second patient.

The point of origin of the cyst in the first case was apparently a portion of the posterior wall of the sinus, which bled from several points when the sac of the cyst was dissected away from the bone.

The evidence of point of origin was not as definite in the second case.

Whether the location of the lesion in the outer aspect of the frontal sinus is significant from a diagnostic standpoint cannot be stated. The similarity of the roentgenologic findings in the two cases is striking. The lesion in the sinus had definite outlines, but defects in the integrity of the bone were not evident. The density of the shadow did not suggest the presence of an opaque lesion, but rather the presence of a mucocele. Microscopic study of the histologic structure of the walls of the cysts can hardly be considered of diagnostic significance, as nothing of particular importance in the determination of the character of the cyst was found. The most that can be said is that the character of these particular cysts is unidentified because the nature of the cysts could not be determined by any means at our disposal. The question of teratoma arises, but evidence of hair, teeth and other structures commonly found in teratomas was not encountered.

The history and clinical findings are not sufficiently different from those encountered in mucocele of the frontal sinus to warrant the suggestion that a definite syndrome can be established. The operative findings, however, were much different from those encountered in cases of mucocele. The operative technic which was adapted in each case proved satisfactory. However, if in patients with similar findings, the history reveals that episodes of severe pain have occurred, cysts of the frontal sinus must be considered in the differential diagnosis.

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XLI

CEREBROSPINAL RHINORRHEA: REPORT OF A CASE PRESENTING HYPEROSTOSIS FRONTALIS INTERNA

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The patient who first notices a discharge of clear fluid from the nose does not feel much concerned about it. He believes that he has hay fever or a beginning cold. When the condition does not respond to home remedies or the discharge becomes more profuse, a physician is consulted. If the physician is not on his toes, the true cause of the symptoms is not recognized and improper therapy, especially of the surgical type, may be instituted with serious consequences.

HISTORY

Miller in 1826 was the first to show that it was possible for the spontaneous escape of cerebrospinal fluid through the nose to occur. This work was preceded by Willis in 1676 and Morgagni in 1762 who reported cases in which a clear fluid was discharged from the nose, but neither the nature nor the reason for the discharge was recognized. Tillaux in 1877 reported a case in which a watery nasal discharge was proved to be cerebrospinal fluid, and in 1883 Leber reported a case of cerebrospinal rhinorrhea in which the cause was supposed to be internal hydrocephalus. In 1899 St. Clair Thomson[15] reported one case of cerebrospinal rhinorrhea and collected eight definite and 12 probable cases from the literature. Schwab and Green reported the cases up to 1905 and added one of their own. They pointed out that optic neuritis usually is seen with this condition.

Locke[12] in 1929 reviewed the literature to date and found reports of 14 cases of fatal cerebrospinal rhinorrhea in which necropsy was performed. Two of these reports were incomplete, and in each of the remaining 12 internal hydrocephalus was found. In eight of these a cerebral tumor was present; two were cases of congenital hydrocephalus in which rhinorrhea developed in early adult life after the fontanels and sutures had closed; and two were of the adult type. In 11 of the 12 necropsies, definite openings between the floor of the anterior cranial fossa and the nasal cavity were found, but in

the 12th case, only a thinning was present, though in that instance the discharge had ceased 13 days before death.

Janson[9] in 1929 reported a case of rhinorrhea in a three-year-old child with congenital hydrocephalus. Friedmann[7] reported three cases, two with a unilateral discharge in which pituitary tumors were found and a third case of hemorrhage into the internal capsule with bilateral discharge which lasted for three days and then disappeared. Learmonth[11] reported a case of unilateral rhinorrhea in which at operation granulation tissue was found in the region of the cribriform plate. Iodine packs were introduced to promote adhesions between the granulation tissue and the dura, and the discharge seemed to have been controlled. Euzière and Vitallefont[5] in 1932 reported a case of cerebral tumor with total blindness of three years' duration in which spontaneous cerebrospinal rhinorrhea for 15 days resulted in some vision, but the patient's blindness returned as soon as the flow ceased.

Donnelly[4] reported a case of spontaneous cerebrospinal rhinorrhea in a woman 60 years of age which appeared following an attack of influenza. This patient awoke every morning with a severe bitemporal headache which disappeared about nine or ten o'clock when the rhinorrhea appeared. The discharge continued intermittently throughout the day and night until the early morning hours at which time the headache reappeared. At first a diagnosis of chronic maxillary sinusitis was made, but further roentgenologic investigation and a study of the discharge revealed the true nature of the condition. An attempt at lumbar puncture was made and a barbital derivative was given for pain. This was followed by signs of increased intracranial pressure and an absence of the discharge. Shrinkage of the upper nasal mucosa resulted in a reappearance of the discharge with relief of the intracranial symptoms. Two years later the patient was in good health with the exception of the discharge.

Wurster[17] in 1937 described a patient with cerebrospinal rhinorrhea of five years' duration who had consulted five rhinologists who failed to make a correct diagnosis. No treatment was given but the patient was advised to beware a beginning cold and to use a mild silver protein preparation in the nose in the event that he felt one approaching. About three years later the discharge ceased suddenly and has not recurred. Intranasal examination revealed no lesions such as granulation tissue. Graham[8] reported a case of rhinorrhea of five months' duration. At operation the openings of the cribri-

form plate were found to be larger than usual. These were filled with bone wax, and the rhinorrhea ceased and has not returned. Friedberg and Galloway[6] applied 20% silver nitrate to a region of the middle turbinate from which fluid could be seen dropping, and in 12 days a rhinorrhea of six months' duration had ceased without any recurrence. Wessels[16] reported a case which showed at operation an area of bone in the anterior fossa which had been completely destroyed. A piece of muscle was placed over this, and there has been no recurrence of the discharge which had persisted for eight months.

There are several theories as to just what happens in these cases. Lawrence[10] mentions that in embryonic life there is an opening between the subarachnoid space and the membranes surrounding the olfactory nerves, and that a sudden increase in pressure forces these channels open. Loftus[13] mentions a defect of the craniopharyngeal canal and, according to his theory, the embryonic canal may be forced open by an increase of cerebrospinal fluid. Locke[12] believes that two factors are necessary for the formation of a fistula between the anterior cranial fossa and the nose. These are: obstruction of the circulation of the cerebrospinal fluid and increased intracranial pressure, brain tumor being the most common lesion in which there is an association of these. When the thin cribriform plate is atrophied and the normal openings in the overlying dura and the arachnoid are enlarged by the increased pressure, leaving only the ethmoid mucous membrane between the cerebrospinal fluid spaces and the nasal cavity, this membrane evidently is unable to withstand the strain thus placed on it and gives way.

Britt reviews the theory advanced by Locke and adds two other routes: 1) openings from a persistent lumen in the olfactory bulb through the cribriform plate into the nose; and 2) an opening from the basal subarachnoid cistern through the cribriform plate into the nose.

Idiopathic cerebrospinal rhinorrhea seems to be very infrequent. A review of the literature reveals only 70 cases reported up to the present.

REPORT OF A CASE

Mrs. S. A. W., aged 56 years, was referred to me because of frontal headache, a sense of nasal obstruction, and a watery discharge from the nose. These symptoms had existed for the past several months. She was being treated by the referring physician for meno-

pause. Examination revealed an obese female, 60 inches tall and weighing 225 pounds.

The conjunctivae, corneas, lenses, and media were clear. The pupils were round, equal, and reacted readily and consensually to both light and accommodation. The optic discs were of normal color and showed no cupping or choking. The blood vessels were of normal caliber. Vision was corrected for near and distant vision. The visual fields did not show any abnormality.

The external canals did not show any abnormality. The tympanic membranes did not show any retraction or bulging and were of normal color.

The frontal and maxillary sinuses were clear on transillumination. The mucous membranes were injected and engorged and a thin, watery secretion was present, being more profuse on the left. Shrinkage did not reveal any polyps. The septum was straight.

The tonsils were atrophic and smooth. The mucous membrane of the posterior wall was slightly injected.

The patient was given ephedrine nose drops to use at home and histaminase in the belief that an allergic condition was present. She returned a week later feeling much better because the sense of nasal obstruction had been relieved, but she still complained of the watery discharge. Local treatment was given in the office, and she returned to her home to continue the same medication as before. She was seen two weeks later and at that time complained very much of the discharge from the left side of the nose, stating that when she got up in the morning and held her head down, the discharge ran from the left nostril. When she held her head forward in the treatment chair for a few seconds, a clear fluid dropped from the left nostril at about the rate of a drop every five seconds. This secretion was collected and sent to the laboratory for examination. The report was: "The specimen consists of about 5 cc. of a watery, colorless, odorless fluid, which is neutral to litmus. Examination reveals four cells per cu. mm. There is no precipitation upon boiling or upon the addition of acetic acid. The fluid reduces Fehling's solution, and quantitatively there are 48 mg. of reducing substance (dextrose) per 100 cc. This analysis is very similar to that of cerebrospinal fluid."

Following this, X-ray views of the skull were made. The report was: "Antero-posterior and lateral views of the skull show no X-ray evidence of fracture of the skull. Suture line markings appear nor-

mal. Blood vessel markings are exaggerated in the middle meningeal groove. There is a marked thickening of the entire cranial vault which is especially noted in the frontal region, involving the inner table, and has the appearance of hyperostosis frontalis interna. There is a marked calcification of the posterior clinoid process which gives the sella turcica a spherical appearance."

The diagnosis of idiopathic cerebrospinal rhinorrhea having been established, the patient was instructed to stop all medication and cautioned at the first sign of a cold to go to bed and to use a mild silver protein preparation in her nose.

COMMENT

The case reported is typical of similar cases of idiopathic cerebrospinal rhinorrhea in that there was a sudden onset without any apparent cause and no other symptoms except the discharge were present. The finding of the hyperostosis frontalis interna gave rise to the question as to whether it was the cause of the rhinorrhea. A review of the literature failed to throw any light upon this matter because no one had reported a similar case in which both conditions were present. Our case showed many of the features of the Stewart-Morel syndrome as far as the X-ray findings, the obesity, the age, and the sex were concerned, but there was a total absence of any mental symptoms. The case reported also showed the alterations of form and structure of the sella turcica described by Pende and reported by Bertolotti.[2]

It has been noted by Moore[11] that the dura is more closely attached to the frontal bone than elsewhere in the cranium and in hyperostosis is so adherent at times that it cannot be loosened. An older theory as to the causation of the hyperostosis, was that it was a compensatory process for filling the space produced by atrophy of the frontal lobes of the brain incident to old age, bringing about a negative pressure between the dura and the inner table. Canavan[3] in a study of hyperostosis frontalis interna did not report the presence of rhinorrhea, but at autopsy found that in the region of the hyperostoses the dura mater was adherent. In fact, a greater part of this membrane had literally been absorbed, and what remnants were visible had a thin, stretched, ribbon-like or shredded appearance. None of our views revealed the region of the cribriform plate so that change here could not be noted.

From the findings in our case we have ventured the opinion that the rhinorrhea could have been a result of the hyperostosis, either due

to an actual tearing of the dura mater in the region of the cribriform plate as Canavan found, or simply to a stretching of the dura due to the hyperostosis and its elevation from the bone in this region.

SUMMARY

1. A case presenting both cerebrospinal rhinorrhea and hyperostosis frontalis interna is reported.

2. A review of the literature failed to reveal a similar case.

3. Another theory as to the cause of idiopathic cerebrospinal rhinorrhea is advanced.

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XLII

ANGIOFIBROMA OF THE LEFT MAXILLARY SINUS*

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DETROIT

In the study of tumors of the nose and throat, nasopharyngeal and nasal accessory sinus neoplasms should be considered as a group because of their pathological similarity. Of the benign tumors in this classification, those composed of connective or vascular tissue, or both, constitute an important subgroup. For purposes of this discussion, it is first necessary to eliminate from this subgroup ordinary capillary and cavernous hemangiomas, common in this region, ordinary nasal polyps, which are actually soft fibromas, and granulomas of an exaggerated type. There remains for our consideration that comparatively small group of solid tumors composed chiefly of mature connective tissue, often richly vascularized, which are described as angiofibromas and fibroangiomas.

The term angiofibroma is not completely satisfactory because it leaves some uncertainty as to whether the lesion is fundamentally a histoid or an organoid tumor. If it is the former, it should be considered a highly vascular or telangiectatic fibroma; if the latter, it is a hemangioma with an unusual amount of fibrous stroma (sclerosing hemangioma). One other possibility is that an angiofibroma or fibroangioma is a mixed tumor composed fundamentally of both vascular and connective tissue. It is not easy to determine the exact histogenesis of these tumors, but fortunately the matter is not of great importance. While definite proof is lacking, the preponderance of evidence favors considering fibroangioma as synonymous with vascular or telangiectatic fibroma. Whether the vascular component is neoplastic, or simply represents a rich vascularity, cannot be decided here.

It is apparent from a perusal of the medical literature that in both diagnosis and treatment angiofibroma and fibroma of the nasopharynx cannot easily be separated. Furthermore, it should be remembered that these tumors, while ordinarily considered benign, may

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under certain circumstances exhibit a tendency to invade and recur, and therefore possess features of local malignant disease. Because of the unsatisfactory state of the literature dealing with this subject, it is impossible to estimate accurately the incidence of this type of neoplasm. According to Friedberg,[1] it occurs chiefly in males between the ages of 10 and 25 years and seems to be related to the growth and maturation of the bones of the base of the skull.

Limiting this discussion to angiofibroma of the maxillary sinus does not greatly change the clinical aspect of the disease except in so far as the treatment approach might be more difficult. Obviously the outstanding characteristic of such a tumor would be a tendency to bleed profusely, either spontaneously or when traumatized. This feature presents an obstacle to making a correct diagnosis. In the first place, an attempt at securing a specimen for biopsy might precipitate severe hemorrhage. In the second place, these tumors are frequently encountered in locations where surgical removal is difficult and requires repeated attempts. Each attempt is, of course, accompanied by severe hemorrhage.

Methods employed in the diagnosis and treatment of angiofibroma or fibroma of the nasopharynx or maxillary sinus have been largely unsatisfactory. Delavan[2] states that he knows of many deaths occurring as a result of hemorrhage and shock either on the operating table or a few days following operation for such tumors. This constant threat of severe hemorrhage as an annoying and stubborn complication to surgical therapy, often with fatal results, makes highly desirable some form of treatment which will control the hemorrhage and facilitate the removal or destruction of all the neoplastic tissue.

The first successful substitute for surgical excision or resection was electrolysis to reduce the size and vascularity of the neoplasm, using preferably the bipolar electrolytic current. More recently radium has been found to be a more efficient physical agent for this purpose.[3]

It is generally agreed that interstitial radium irradiation is the preferred method. However, when a tumor of this type occurs in a comparatively inaccessible location, such as the maxillary sinuses, and is accompanied by very profuse hemorrhage, it may be necessary to resort to contact irradiation. In either event, the radium has two effects on the tumor: vascularity is reduced and fibrous replacement of the vascular tissue is brought about. The use of irradiation in the treatment of hemangiomas and lymphangiomas is well known. The desired result is produced by damaging the endothelial lining of the

vascular spaces and subsequent production of thrombosis, thus obliterating all or part of the vascular channels. The larger the vascular spaces, the more readily is thrombosis produced. Eventual organization of the thrombi leads to fibrosis. The physical result, therefore, while characterized by some shrinkage, is really fibrous replacement of the vascular tumor rather than its destruction. A mass usually remains after the irradiation therapy, necessitating final surgical removal.

It is somewhat more difficult to visualize the effect of radium on the connective portion of the neoplasm. Judging from the results obtained in the case reported here, as well as from the experience of others, the radium irradiation accomplishes both reduction in the size of the tumor and diminution in its vascularity. Because it is not necessary that these tumors be entirely removed by surgery, radium therapy is quite likely to be adequate. If subsequent surgical removal of the altered mass is considered necessary, surgical diathermy (endothermy) would seem to be the method of choice.[1]

REPORT OF A CASE

A 15-year-old boy was admitted to the hospital on March 27, 1940, complaining of almost constant colds and frequent nosebleeds over a period of five years and a gradual but very noticeable enlargement of the left side of his face over the same period of time He had been struck across the face by a baseball bat when he was seven years old, but had had no difficulty until three years later while attending a summer camp, where he experienced several spontaneous nosebleeds. Intermittent bleeding persisted for four to five days and always came from the left side of the nose. Since then he suffered from epistaxis about once a month. When his head colds were severe there was swelling and tenderness over the area of the left maxillary sinus. The left side of his face gradually became larger than the right. On four different occasions during the past five years the patient had nasal polyps removed at another hospital and his nose had twice been cauterized for bleeding points. A tonsillectomy and adenoidectomy had been performed when the patient was six years old. The maternal grandfather died of cancer of the throat. The family history was otherwise unimportant.

Physical Examination: At the time of admission to the hospital the patient weighed 102 pounds (46.4 kg.) and appeared to be in fairly good health except for the enlargement of the left side of the face and an adenoid facies (Fig. 1). The left eye was somewhat prop-

Fig. 1. Appearance of the patient when he was admitted to the hospital.

tosed. Examination of the blood gave a value for hemoglobin content of 87% (13.5 grams); there were 4.42 million red corpuscles and 5900 white corpuscles per cubic millimeter, of which 60% were polymorphonuclear neutrophiles, 38% lymphocytes and 2% eosinophilic neutrophiles. Roentgenographic examination (Dr. J. E. Lofstrom) revealed the left maxillary sinus to be enlarged to eight times its normal size, with the mesial wall crowded against the septum and completely filled with a tumor mass (Fig. 2).

On the day following admission (March 28) a Caldwell-Luc approach was made in an attempt to explore the left maxillary sinus, but as soon as the thickened wall of the sinus was punctured, such profuse hemorrhage occurred that a tumor which was encountered could be only partially removed before a pack had to be placed in the cavity and held under pressure. During this short operative procedure the patient lost approximately 500 cc. of blood. He was given a blood transfusion, and it was decided to remove the remainder of the tumor later. The pathological examination of the tissue removed showed the tumor to be an angiofibroma. Two days later the

Fig. 2. The left maxillary sinus at the time of the patient's admission to the hospital was enlarged to eight times normal size and completely filled with a tumor mass. The right maxillary sinus in this patient is smaller than average size.

left external carotid artery was ligated. Surprisingly this had no effect on the hemorrhage. The wound had to be kept tightly packed, and another blood transfusion given. The hemoglobin content of the blood had fallen to 52% (8 grams), with 2.55 red blood cells per cubic millimeter. During the next ten days there was constant oozing of blood, but the packs were changed only when they developed a foul odor or the patient's temperature became elevated. Each time they were changed the patient was given an anesthetic, and each time so much blood was lost that it was necessary to administer another blood transfusion.

Pathological Description: The sections consisted of neoplastic tissue with a surface of ciliated transitional epithelium. The tumor was homogeneously composed of irregular vascular spaces, variable in size, containing blood. The walls of these vessels consisted entirely of a single layer of endothelial cells. These neoplastic vascular spaces were imbedded in and widely separated by an abundant stroma com-

Fig. 3. Photomicrograph of the tumor.

posed of young fibrocytes and fibroblasts. The stromal cells were fully differentiated. While the stroma was fairly cellular there was, between the connective tissue cells, a large amount of fibrillar connective tissue. Fibrosis was not a feature, and mitotic figures were not present. The neoplastic character of the stroma was not consistent with a diagnosis of sclerosing hemangioma but supported the belief that the lesion was an angiofibroma. (Dr. Osborne A. Brines.)

Roentgenographic examination of the sinuses on April 10 showed the lateral inferior wall of the orbit to be destroyed as well as the lateral and posterior walls of the antrum, but there was no evidence of the tumor's extension into the area. Inasmuch as ligation of the left external carotid artery on March 30th had not reduced the amount of hemorrhage, the right external carotid artery was ligated on April 11th in the belief that the collateral circulation might have been so great as to constitute an important source of blood supply to the tumor. Again there was no apparent retardation in the bleeding. Further surgical removal of tumor tissue was still impossible, and endothermy was likewise out of the question. On April 16th, 50 mg. of radium in a single capsule 2.5 cm. in length with a 1 mm. brass wall, were inserted for ten hours, or a total of 500 mg. hours, as an initial dose. After ten days, the same capsule was inserted for twelve hours, or a total of 600 mg. hours of irradiation. Bleeding continued and it was decided that additional

contact irradiation should be given. Fourteen days after the first application of radium, the same capsule was placed in contact with the tissue for twenty-four hours, or 1200 mg. hours of irradiation. This provided a total of 2300 mg. hours within a two-week period.

There was no evidence of facial anemia despite both external carotid arteries being doubly ligated. The patient was failing rapidly, however, and was receiving his only nourishment from blood transfusions. While waiting for the hemostatic effect of the radium, it was obvious that something further must be done to check the persistent bleeding, as the patient was slowly exsanguinating himself despite frequent blood transfusions. On May 7th the left common carotid artery was ligated slightly below the bifurcation. Still there was no appreciable diminution in the hemorrhage, and endothermy could not be used. No clinical evidence of cerebral anemia resulted from this procedure, but the patient continued to grow weaker. Between March 28th and May 12th he had lost 60 pounds (27.3 kilograms) in weight. On May 12th examination of the antrum showed no tumor tissue remaining, and it was now possible to see an abberant blood vessel in the floor of the antrum. This was crushed successfully, but there was still a moderate amount of bleeding from the lateral wall, far back toward the ear. Endothermy could now be used for a final elimination of the remaining mass. As there was practically no medial or posterior wall remaining, a direct view was obtained into the oropharynx and nasal cavity. The depth of the opening extended to the floor of the cranium posteriorly. The tumor had extended back through the ethmoids and well into the sphenoidal area beneath the orbit. During this operative procedure the patient lost very little blood and the packs were replaced loosely.

Thereafter the patient improved rapidly. He received a high-caloric, high-vitamin diet and gained weight steadily. Subsequent recovery was uneventful, and on the 70th hospital day the patient was discharged. On the day of discharge his hemoglobin had risen to 68% (10.5 grams). During his hospital stay he had received 11 liters of blood in 23 separate transfusions, or an average of 500 cc. every third day.

The patient was seen on January 23, 1941, and no tumor tissue was recognized at this time, but there was evidence of fibrosis in the wall of the cavity. Roentgenographic examination showed an area of decreased opacity involving the entire left antrum. On April 17th the patient was again admitted to the hospital, and the aperture in the canine fossa was closed.

There is now a loss of osseous structure medially and inferiorly. The patient will always have a large opening from the sinus directly into the nasopharynx and some loss of function of the left nasal cavity with some crust formation because of the loss of turbinates. Despite the ligation of three principal arteries supplying blood to the head, the patient's color is good, and he appears to be well and normally active. He now weighs 116 pounds (52.7 kilograms). The hemoglobin content of his blood is 75% (11.5 grams), with 338 million red corpuscles and 8000 white corpuscles per cubic millimeter. There is no noticeable deformity of the face, although there is some malformation of the dental arch due to the patient's previous history of mouthbreathing. There has been no recurrence of the tumor in ten months and the prognosis appears to be very good.

SUMMARY

A case of angiofibroma of the maxillary sinus is reported in which the final treatment result was wholly satisfactory.

The usual anticipated mechanical obstacle to treatment in the form of extensive hemorrhage due to the vascularity of the tumor was encountered.

An unusual feature of this case was the fact that ligation of both external carotid arteries and the left common carotid artery was accomplished without untoward incident to the patient.

Radium therapy was apparently the important part of the treatment in this case, inasmuch as the surgical therapy consisted of little more than a biopsy.

Theoretically an ideal method of treating such a tumor would be immediate complete removal by surgery. This, however, is rarely a practical possibility. Biopsy, although dangerous in such a vascular lesion, is, I believe, necessary to furnish an accurate diagnosis leading to intelligent treatment.

Angiofibroma is an uncommon tumor generally and a particularly rare lesion in this location. It is a neoplasm which is difficult to classify histologically. This feature has been discussed at length.

The clinical absence of disease in this patient ten months after treatment would seem to indicate that recurrence is now a very remote possibility.

2201 Jefferson Avenue East.

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XLIII

(From a Group of Case Records Collected and Abstracted Under the Title of "My Most Interesting Case," By Noah D. Fabricant, M.D., Chicago)

SUBACUTE FRONTAL SINUSITIS

O. E. Van Alyea, M.D.

Chicago

B. H. was first seen in my office March 11, 1937, complaining of a daily, foul-smelling discharge from the left side of his nose. The infection, located in the left frontal sinus, had existed for six months and could be traced to a concomitant left antrum infection of dental origin. The antral infection had cleared up following a fenestration operation a few months previously.

Examination revealed a high deviation of the nasal septum to the left which impinged on the middle turbinate, pressing it against the lateral nasal wall. Pus was present in the middle meatus. Following shrinkage and anesthesia, a frontal cannula was passed between the turbinate and the lateral wall. This entailed some difficulty, although once accomplished, the frontal ostium was easily engaged by the cannula tip. Irrigation revealed a considerable amount of foul-smelling pus of pea-soup consistency.

On April 6, 1937, a resection of the septum was performed, and this permitted an infraction of the left middle turbinate.

Recovery from the operation was rapid. There was very little tissue reaction, and a wide open middle turbinate resulted. Lavage of the sinus a few days later produced a similar result to that of the first irrigation. These treatments were repeated daily with a gradual diminution of the odor and quantity of pus returned. With the seventh irrigation, no odor was present, and with the sixteenth, the returned solution contained only a small clump of muco-pus. The patient was next seen a week later. The sinus was negative on irri-

gation, and he was entirely free of symptoms. He has reported at intervals during the past three years that he has had no subsequent attacks of sinusitis and no return of the discharge.

This case illustrates the efficacy of irrigations in the treatment of the subacute type of frontal sinusitis.

Perhaps fully as important as the irrigations is the enlargement of the drainage area of the sinus where it is indicated. It has been shown in other similar cases that one of these therapeutic measures without the other may result in failure. A combination of the two, however, embraces an essential principle of surgery, to-wit, the removal of purulent material and the restoration of the natural pathways of drainage.

It must be borne in mind that all cases of long standing frontal sinusitis do not respond to irrigation therapy. When tissue changes take place in the sinus lining membrane, more radical procedures may be found necessary.

Most acute attacks of frontal sinusitis will clear up spontaneouslv with little or no treatment between the fifth and tenth days. The frontal ostium located in the most dependent portion of the floor functions adequately in the normal case as a drainage outlet to the sinus. In the acute state, engorgement of the tissues causes a partial or complete occlusion of its lumen. As the swelling subsides, the ostium opens and the symptoms disappear.

Persistence of the infection beyond this stage is usually indicative of some structural defect in the drainage areas.

Often overlooked as a cause of defective frontal sinus drainage are encroaching frontal and ethmoid cells. In approximately 25% of all cases a cell is present in or near the frontal sinus which either overhangs or encroaches in some manner on the frontal ostium.

This factor perhaps accounts for a persistence of a frontal sinus infection in fully as many cases as does the blocked middle meatus due to a bulky or misplaced middle turbinate.

135 S. LaSalle St.

DISCHARGE FROM CHRONIC FRONTAL SINUSITIS DRAINING DIRECTLY INTO THE MAXILLARY SINUS

HAROLD I. LILLIE, M.D.

ROCHESTER, MINN.

Among the unusually interesting clinical problems referable to disease of the paranasal sinuses that stand out in my memory was a case encountered in 1926. A male patient, aged 38 years, came to the Mayo Clinic complaining of "chronic sinus disease", which had persisted over a period of three years. The symptoms complained of were pain under certain conditions and excessive discharge. Several operations had been performed, and the pain had not been relieved. The discharge at times was very malodorous. The symptoms were referred to the right nostril.

Examination revealed that there was a small window opening into the right maxillary sinus; the right middle turbinate had been partially removed, and the ethmoid cells had been entered. Thin, mucopurulent discharge was present in the middle meatus. Roentgenographic examination revealed the right maxillary sinus and the left frontal sinus to be clouded. Observation over a period of time led to the suspicion that the right maxillary sinus contained a secondary pocket that had not been encountered at the time of the previous operation elsewhere. An external operation was decided on.

The operation revealed such a pocket in the lateral aspect of the maxillary sinus just under the floor of the orbit. It was felt that this finding accounted for the symptoms and signs. However, following operation the symptoms and signs did not disappear. There continued to be much discharge in the maxillary sinus each day. It was noted that after the discharge had been removed it was again encountered in considerable amount within a few hours. Because a probe could be passed into what appeared to be the nasofrontal duct and no discharge was obtained on ventilation, it was not suspected that the maxillary sinus was acting as a reservoir for discharge from the frontal sinus. The roentgenogram of the right frontal sinus appeared to be normal. Still there was too much discharge to be accounted for by the maxillary sinus on which operation had been performed. An exploratory operation on the frontal sinus was decided on because there seemed to be no other reason by which to

explain the clinical picture even in the face of apparently negative findings.

At operation it was found that the frontal sinus contained thick, pyogenic membranes with foul-smelling pus, and the fronto-ethmoidal cells showed the same pathologic changes. What was more interesting was that when the stage in the operation of fashioning an opening into the nose was reached it was found that the real nasofrontal duct emptied into the maxillary sinus. Why roentgenographic findings were apparently negative is not easy to explain. The previous successful probing of the frontal sinus had really entered an uninvolved cell over the bregma.

Following this latter operation all symptoms and signs were relieved. The patient was seen in the summer of 1939, and he reported that he had had no further trouble with his nose.

THE MAYO CLINIC.

ABSCESS OF THE TONGUE

SAMUEL SALINGER, M.D.

CHICAGO

S. C., aged 40, complained of a sore throat for several days past in which the outstanding subjective symptom was pain on swallowing. Examination revealed cervical tenderness at the angle of the jaw on the right side and slight redness of the pharynx, pillars, base of the tongue and right pyriform sinus. Since the local findings seemed inadequate to explain the severity of the pain, it was difficult at this time to make a diagnosis. The patient was instructed to use a hot gargle frequently and apply heat externally. He was seen again two days later at which time the picture was more clear. The pain had increased; the right half of the tongue was larger than the left and in its posterior half seemed pushed upward toward the palate. On account of the pain, it was impossible to hold the tongue for a mirror examination nor was a direct laryngoscopy possible for the same reason. Palpation over the dorsum of the tongue elicited marked tenderness as did pressure against the tongue in the floor of the mouth on the right side. Under local anesthesia an incision was made into the lingual aspect of the tongue on the right side opposite

the first molar tooth and the blade of the knife directed downward and backwards toward the base. The abscess cavity was entered at a depth of 3.5 cm. and a large amount of foul pus evacuated. A small rubber tube was inserted for the first 24 hours after which the cavity was packed lightly with gauze. Recovery was uneventful.

Since the etiology of the infection was unknown we can only assume that it was most likely due to some minor trauma such as might be caused by a fish bone, tooth brush bristle or other small puncturing foreign body. Abscesses within the tongue are rare although abscesses in the immediate vicinity are not uncommon. We have all at some time or other seen an abscess in the floor of the mouth due to infection of the sublingual or submaxillary gland, abscess of the vallecula due to trauma or during an attack of influenza, and abscesses in the pyriform fossa from a variety of causes.

The case just reported was confusing at first because the pain was more severe than the local findings could explain, and the diagnosis was made only when the tongue became tender to pressure on application of a tongue blade during the examination. Even then we could not be sure we were not dealing with an abscess of the vallecula since it was difficult to hold the tongue for a mirror examination. However, when the base of the tongue began to rise there was no longer any doubt. It is interesting to note that the pressure from below in the submental region gave little or no reaction nor was there any swelling in the hyoid region, demonstrating again how resistant the mylohyoid muscles and investing fascia are. Seldom does an abscess below or above this plane ever tend to break through in the opposite direction.

25 E. Washington St.

EXFOLIATION OF THE COCHLEA, VESTIBULE AND SEMICIRCULAR CANALS

Max A. Goldstein, M.D.

St. Louis

It is nearly a half century ago that I observed a case of exfoliation of the cochlea, vestibule and semicircular canals. The case herewith described may, perhaps, in consideration of the size of the sequestra and the numerous clinical phenomena, deserve a recognition with the rarest cases of necrosis of the labyrinth.

In 1892 a four-year-old colored boy had an acute earache which was followed by a copious purulent discharge. For 18 months the discharge continued freely and uninterruptedly without the accompaniment of any unfavorable symptom. In July 1894 the patient was admitted to the old Missouri Medical Polyclinic. His general condition and the suppurative process had now assumed a decidedly unfavorable aspect. The discharge had stopped because of plugging of the entire external auditory meatus by a cheesy mass.

There was considerable induration of the post-auricular region with distinct points of fluctuation. This was incised and drained and about one and one-half ounces of green, fetid pus obtained. A marked and almost complete facial paralysis was demonstrable on the affected side. A small sinus was present, about one-half inch posterior to the insertion line of the auricle. On August 5th, the patient was prepared for operation. I made a long, free incision, connecting the upper posterio-auricular abscess opening with the orifice of the sinus. A free opening to the bone was made. Placing a curette in position, preparatory to the removal of the necrotic bone mass, I observed a serious condition; the entire area was one rotten mass. I then exposed the sinus and completed the operative procedure.

The following day I removed the first dressing. The discharge was profuse and the odor excessively fetid. After the second dressing it was noticed that the motor paralysis of the right eye had partially subsided and that the patient was now able to close the eye almost completely. The dressings were changed daily for three months with but slight change in the general appearance of the wound or patient. Throughout the entire course of treatment there was no pain, tinnitus, vertigo, nausea, vomiting or febrile reaction.

Early in November a change was noted—the patient became restless, peevish and drowsy. On redressing the wound I noticed for the first time a necrotic mass of bone, black in color, rough in appearance, projecting from the anterio-lateral wall of the posterior auricular sinus. The discharge was profuse and intensely fetid. The black necrotic mass was removed through the fistulous opening. For several days, the general condition of the patient improved, but again it was necessary to remove a second sequestrum, and some days later, a third sequestrum.

On November 15, the patient began to cough—a hoarse, short cough with frequent expectorations. Microscopical examination of the sputum revealed numerous tubercle bacilli. A new sequestrum was seen, and this was removed from the posterior sinus. The patient

became lively and talkative, although he was considerably emaciated and his cough very harassing. It was obvious that I was dealing with a rapidly developing miliary tuberculosis. However, by far the most interesting and important factor which presented itself was the existence of hearing on the affected side after the removal of the cochlea and the deep structures of the petrosa. Next in importance was the preservation of the equilibrium and balance of the patient. Terminally, the only cerebral symptom was a mild stupor. Progressive emaciation and prostration developed, and the patient died on January 29th.

Unfortunately, permission was not granted for a complete autopsy. Examination of the affected temporal bone corroborated my description of the necrosed and exfoliated areas. Circumscribing the region of the osseous external auditory meatus, and involving the mastoid and squama, was a necrotic zone with irregular but well-defined margin. A cone-shaped sinus extended into the eustachian tube and was filled with granulations. All landmarks of the osseous external auditory meatus and the cavum tympanum had disappeared. After removal of the bone, the dura was found at all points to be perfectly firm and intact. The most careful and detailed search failed to reveal any meningeal lesion whatever.

In conclusion, it may be remarked that in a case of miliary tuberculosis, with the primary infection an aural one of long standing, and a necrosis, which by its extensive bone destruction, exposed to direct contact with the specific suppurative processes the largest portion of the temporal lobe, lateral sinus and temporal section of the internal carotid artery, the absence of any meningeal or cerebral complications must indeed be considered a rare occurrence.

4574 W. Papin St.

CONCERNING CERTAIN HEARING PHENOMENA

Edmund Prince Fowler, M.D.

New York

Although it may not be so dramatic as many surgical experiences, the following, from the standpoint of the unexpected and for far-reaching implications, was unique in my experience. It concerns certain hearing phenomena.

In 1921 and 1922, at the beginning of reliable audiometric testing, attention was called to marked troughs in the hearing curves of some ears and particularly to sharp drops in the upper half of the frequency range. In order to explore the auditory characteristics of these deafened areas, many experiments were tried. In fact, any that came into my head were tried a few times to see what—if anything—happened! One of the stunts was to have the patient listen to various sounds at different loud intensities, the object being to detect any changes which occurred in the quality of the sound.

One of the first patients subjected to these procedures had a decided loss of hearing in the frequencies above 2048, the greatest loss being at 4096.

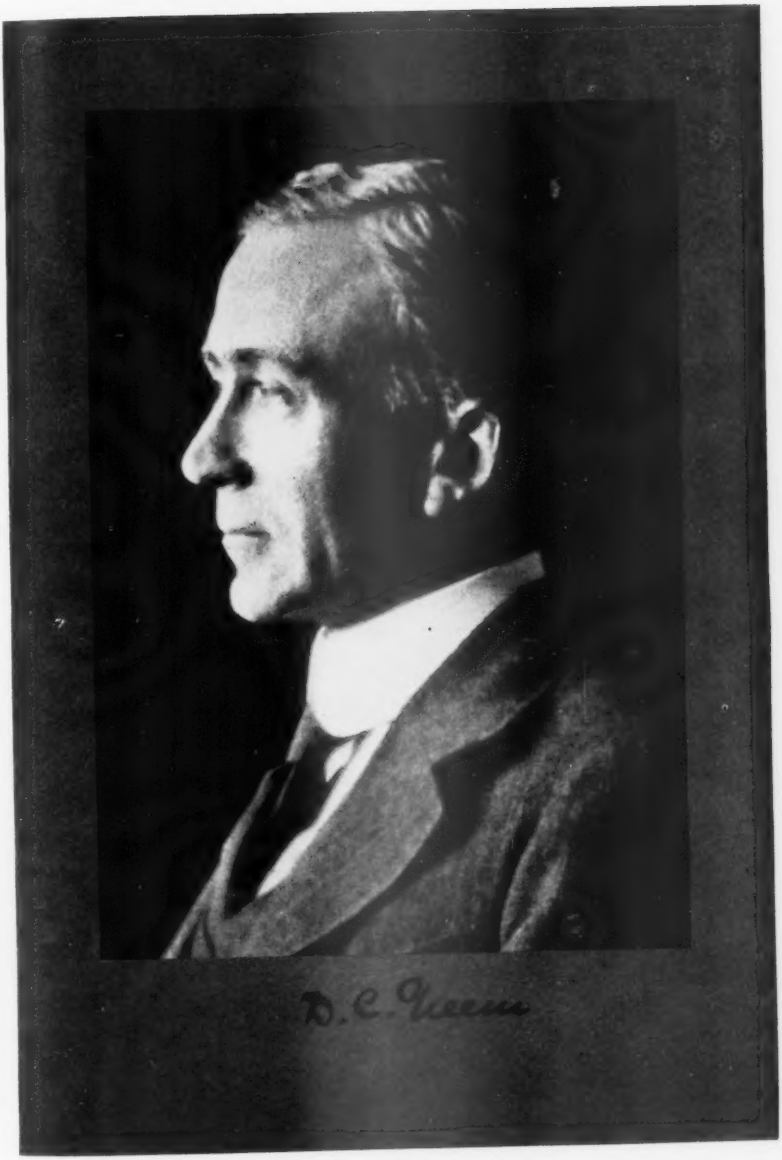
When asked the usual questions about timbre, frequency and intensity changes, etc., he informed me that the sound in the poor ear appeared very loud although the dial on the audiometer was set only 10 db. above his threshold in this ear. This led to comparing it with the sensation of loudness made by the same intensity in the opposite ear, as obviously here was offered a simple means for estimating loudness sensation in the deafened ear. Much to my surprise, the patient stated that when the intensity in the poorer ear was raised from 30 db. (its threshold of hearing) to 30 db. above its threshold, or in other words to a setting of 60 db. above average normal threshold, the sound appeared just as loud as a similar intensity in the opposite normal ear. At first this appeared absurd. I thought that the audiometer or one of the receivers had become deranged. However, this was not the case. Subsequent tests on hundreds of people proved that this phenomenon occurred in every monaural or unequal binaural nerve deafness, as diagnosed by losses in bone conduction by the functional tests and by clear-cut and marked bone conduction losses at the frequencies responding in this way to loud sounds.

An explanation of the pathologic physiology of the phenomenon was not obtained at this time, although several hypothetical explanations were available. The whole thing was very mystifying. Later, Lorente de No stated that careful thought concerning the known anatomical and physiological facts about the neural mechanism of the body reveals a simple explanation. In fact, all nerves act in this way because of the multiple and overlapping connections of the terminal dendrites.

Every nerve fibre in the cochlea and the auditory centers is connected with several cells, and every cell is connected with several

fibres. Moreover, nerve fibres cannot carry impulses higher than a certain limiting frequency. Furthermore, in general, the intensity of a stimulus is determined in great part by the frequency of the impulses carried by the nerves. There is then a limiting frequency of impulses and a limiting intensity of each localized stimulus. If then a number of hair cells or a number of fibres in the cochlea nerve are missing, near threshold tones will appear weak, but loud tones will activate more strongly the hair cells or cochlea fibres. They will stimulate (excite to limiting intensity) the remaining nerve fibres or nuclei, so that the cortex may well receive the same number of impulses per second from a deafened ear as from a normal ear. The sound will appear as loud in the diseased ear as in the normal or less affected ear. Bone conduction may be lowered by certain obstructive lesions as well as by neural lesions. The phenomenon may be employed to differentiate these lesions. In fact, the phenomenon is pathognomonic of neural deafness.

140 E. 54TH ST.


D. C. Greene

D. CROSBY GREENE, JR.

1873-1941

Daniel Crosby Greene, Jr., a familiar figure in American laryngology in the early years of the present century, died on April 5, 1941, at Newton Center, Massachusetts.

Doctor Greene was born in Kobé, Japan, January 29, 1873. His father was a missionary, and the family lived in Japan until Greene was 13 years of age. He attended Newton High School and later Harvard College, from which he was graduated in 1885. He received his medical degree from Harvard in 1899.

After an interneship in the Boston Children's Hospital he began the study of laryngology at Boston under Dr. Algernon Coolidge, and held various positions in the Out-Patient Departments of the Massachusetts General Hospital and the Boston Children's Hospital.

He was a member of the American Laryngological Association and its vice-president in 1917; of the American Laryngological, Rhinological and Otological Society; the American Bronchoscopic Society; the Society for Cancer Research; and the Massachusetts Medical Society.

During the First World War he served as captain in the Medical Reserve Corps.

In 1904 Doctor Greene married Miss Marion Lockwood of Arlington, Massachusetts, and to them five children were born.

In the earlier days, his interest lay chiefly in the diseases of the larynx and the esophagus, and with the advent of modern endoscopy it encompassed also the problems of that art. With few exceptions, therefore, his publications deal with the larynx, many of them with the management of cancer in that region.

Doctor Greene, during his active years, took a prominent part in the deliberations of the various societies with which he was affiliated and made many warm friends.

A. W. P.

L. W. Mapes

MARKUS HAJEK

1862-1941

Professor Markus Hajek, distinguished Viennese laryngologist, died in London on April 12th, the last survivor of a famous group of professors who constituted the fountain head of the specialty during the last generation.

Before the First World War no American laryngologist could feel that his education was complete who had not spent at least a year in the Vienna clinics. These dated back to the beginning of the specialty—in fact since Türck in 1858 demonstrated the clinical application of Garcia's mirror. An English colleague, writing in the British Medical Journal, describes the early days of the clinics as follows: "Türck instructed Morell Mackenzie in the new art, and his beautiful album of water-colour drawings of the laryngeal conditions it rendered visible were piously shown to successive generations of students down to our own days. He was succeeded by such pioneers in the art as Schrötter, Stoerck, and Chiari. When the two chairs of laryngology were amalgamated with the two of otology—made famous by the work of Politzer and Gruber—one of the clinics of otolaryngology was put under the direction of Hajek and the other under the popular and successful Neumann, who died recently in New York, also, like Hajek, an outlaw and an exile from their beloved Vienna."

Hajek began his study of laryngology under Schnitzler, whose daughter he later married and whose son was the popular dramatist, Arthur Schnitzler.

His early contributions were anatomical and supplemented the work of Zuckerkandl and Onodi, and throughout his life many of his lectures dealt with the regional anatomy of the upper respiratory tract. The nose and the paranasal sinuses were the subject of his special interest, and his anatomical demonstrations from a large collection of specimens constituted the basis of many a laryngologist's training. His published volumes on the nasal accessory sinuses and on the diseases of the larynx are classics and have been translated into several languages.

St. Clair Thomson writes that so long ago as 1928, when Hajek delivered the Semon Lecture in London, he sensed the approach of the second great war and feared even then that his country would

be engulfed by either Germany or Russia. When the blow fell and the persecution of the Jews began, his former pupils and colleagues in England, Canada and America enabled him to reach London with his wife. Stripped of all his possessions (he was allowed to bring with him ten marks) he still managed to rescue a few of his original anatomical specimens, which he presented to the Museum of the Royal College of Surgeons.

While he found some cheer in the hospitality extended by his English friends, his health was broken and he did not long survive.

In concluding his appreciation of this great teacher, Thomson is moved to observe: "It is distressing to think that the last two professors in what used to be the most famous school of laryngology in the world were driven from Vienna to die in exile. We have some little comfort in recollecting that they found welcome shelter in the two great democracies."

The passing of this man marks not merely the end of a human life but the end of an era in laryngology.

A. W. P.

Society Proceedings

JOINT MEETING

MIDDLE SECTION OF THE AMERICAN LARYNGOLOGICAL, RHINOLOGICAL AND OTOLOGICAL SOCIETY

AND THE

CHICAGO LARYNGOLOGICAL AND OTOLOGICAL SOCIETY

January 27, 1941

An Evaluation of Meniere's Syndrome

WILLIAM E. GROVE

(This paper is printed in full in the ANNALS, 50:55 (March) 1941)

DISCUSSION

DR. T. ROY GITTINS: Dr. Grove has covered the subject of Ménière's syndrome in the usual complete manner so characteristic of all his writings. I am glad that he has emphasized how little is really known concerning the nature and location of the possible pathology responsible for this syndrome, and also emphasized that many of the symptoms are more suggestive of involvement of cortical or subcortical areas in the brain, than of the inner ear itself. He has also stressed the point that allergy should be given more consideration as a causative factor in this syndrome. I have followed the literature carefully for many years in relation to the subject of vertigo and associated symptoms, and have found that the essayist is one of the few otologists who have given much attention to allergic or vasomotor possibilities in the production of this syndrome.

In the short time at my disposal in this discussion, I wish to lay stress on the characteristics and prevalence of what I choose to call,

for want of a better name, the vasomotor type. An allergic or vasomotor reaction, possibly of a biochemical nature in the tissues of the inner ear, auditory nerve or brain tissue would naturally be a transient upset in the physiology rather than a real pathologic process. History, then, must take precedence over operative or postmortem evidence in the differential diagnosis of everyday practice.

Attacks of real rotary vertigo with pallor, cold perspiration, nausea, and vomiting may appear as prodromal symptoms in an attack of migraine. What is of more importance, however, is that this symptom complex replaces the entire migraine or vasomotor syndrome in many patients for months or years. Such attacks are typical of the classic Ménière's syndrome except that tinnitus and loss of hearing are usually not present. These attacks, because of their short duration and lack of after effects, though they are common, are seldom diagnosed properly. Rarely does an otologist see such patients during their attacks and rarely does the general physician who does see them consider the real nature of the disturbance. The diagnosis is usually heart trouble, acute indigestion, or food poisoning. Because the appearance of the patient and the gastrointestinal symptoms, especially vomiting, are dramatic, little attention is given to the causative vertigo by the patient or the physician. As a rule, the general physician or internist does not need to give much thought to the actual nature of the disturbances, because the attacks are usually of short duration and the patient may be up and around as well as ever in an hour or a day. Occasionally, the attacks occur at intervals for a week or more, especially on sudden changes of position. The patient usually recovers quickly, regardless of, and usually in spite of, the treatment advised.

I have seen but few patients during their attacks, but have heard of a great many while taking routine histories from patients who come to the office because of periodic headache or neuralgia of the vasomotor type. In only three instances have I seen rotary nystagmus; but in these instances it was typical of irritative labyrinthitis during the short time it was present. For over two years, vertiginous attacks of short duration with pallor, cold perspiration, and nausea replaced my own migraine syndrome; and I assure you that a patient suffering from this condition has reason to be seriously disturbed and anxious to be assured that there is probably no real pathology in the inner ear or brain. Very little has been said in the literature concerning this type of Ménière's syndrome (or possibly pseudo-syndrome) but I feel after interviewing patients with peri-

odic vasomotor headaches for many years that it is more common than any other form of vestibular disturbance. Occasionally, of course, a patient may have chronic progressive deafness and tinnitus coincidentally with a tendency to vasomotor upsets. In such instances, differential diagnosis is naturally a real problem, and time may be the most important factor in the final decision.

In my experience, it is rare to obtain a history of vertiginous attacks from the real allergic individual, such as the sufferer from hay fever or asthma. It is not rare, however, to obtain such a history from the individual who has suffered periodically for years with headaches or neuralgia of the migraine or vasomotor type. Whether or not migraine and other types of periodic vasomotor headache usually have an allergic basis, I still think is open to serious question, notwithstanding some very enthusiastic reports in the literature, especially in relation to food sensitivity.

Dr. Grove has stressed the important point of spontaneous remissions in Ménière's syndrome; and certainly the vasomotor type which I am discussing has the same tendency to spontaneous relief as we see in all types of vasomotor disturbances, especially headaches and neuralgias. The results from treatment of any of these conditions should be evaluated with the thought in mind that spontaneous recoveries from any syndromes, at least in my own experience, are more common in the vasomotor individual than after all treatments and operations combined. In my limited experience, good results with low sodium and water intake and ammonium chloride therapy have been very poor in the vasomotor type of this syndrome, much poorer than in the more classical type which probably has real pathology in the inner ear or auditory nerve.

Finally, I wish to stress again my belief in the great prevalence of vertiginous attacks with associated symptoms which are probably of vasomotor and transient origin. I also want to stress that otologists will not necessarily realize how great is this prevalence unless they carefully inquire into the histories of the patients who come to them because of periodic headache or neuralgia. Such patients rarely volunteer any history relative to the vertiginous attacks because they have felt, and have been told in most instances, that such disturbances were in the domain of the general physician or internist, because of the gastrointestinal and other general symptoms.

I am glad to say that I have very much enjoyed reading, studying and hearing Dr. Grove's paper, and I also wish to express my

appreciation of the opportunity to enter into the discussion of this very intriguing disease, syndrome or pseudo-syndrome.

Concerning the symptomatology, very little has been added through these many years since the classical treatise by Ménière. Concerning the actual nature and location of the process, be it biochemical or pathologic, which accounts for the symptoms, very little also has been added through these same years, except possibly in a negative way.

Dr. John Shea: I think we have all enjoyed Dr. Grove's presentation of a subject to which often a whole evening is given, and at the end not much more is accomplished than he has said. I merely wish to add a little about the question of histamine therapy. During acute attacks when the patient is bedridden, histamine will relieve him more quickly than anything we have tried. You may test your patient out by giving .5 cc. histamine diphosphate and, if he does not get any reaction, then 1 mg., and it really works a miracle. It may be repeated in two, three or four days if necessary, and then one must sustain it by giving .5 cc. twice a week. This year at the American College of Surgeons' meeting, Dr. Bayard T. Horton of Mayo Clinic presented histamine as compared to surgery. When surgery can offer only 75% of cures while histamine is so satisfactory, it should first be given a worthy trial.

Dr. Harold I. Lillie: Dr. Hunter Sheldon observed that one patient, in addition to having been relieved of a histaminic headache, also was relieved of the vertigo of which she complained when histamine had been administered intravenously. I think this group of patients is linked up with vasomotor syndromes suggestive of an allergic causative factor. Some patients do well when torantil (a water-soluble, pulverized protein prepared from the mucous membrane of the small intestines) is administered. It is not felt that the treatment is curative. It is really the treatment for an attack, and if maintenance treatment is carried out as Dr. Shea said, the probabilities are that these patients will be relieved.

Another treatment was suggested by an old practitioner. He told me that if he gave 1/75 or 1/50 gr. (0.0009 or 0.0013 gm.) atropine sulfate, most patients suffering from acute attacks of vertigo would be relieved. That probably is explained on the basis of an effect on the vasomotor system, and it is probable that that type of vertiginous attack is caused by some disturbance of the vascular system that atropine overcomes. I have a great deal of respect for the knowledge of practical therapeutic measures that general practitioners possess.

There are toxic types of vertigo. One from which I suffer, especially if I am tired, is the cumulative effect of smoking. I have found that it is relieved usually by taking about two fluid ounces (60 cc.) of bourbon whiskey.

Portmann's operation has not been mentioned as a method of treatment for vertigo. I recently saw a patient on whom that operation had been performed; it was followed by complete relief.

We are on the threshold of learning more about vertigo and its causative factors. I would not subject myself to an operation on the eighth nerve to relieve vertigo until all other methods of treatment had been tried, although I have seen several dramatic results from that treatment. We must not overlook the fact that complete physical and laboratory examinations must be made on all patients who complain of vertigo in order that the general condition of the patient may be known before any method of treatment is instituted.

DR. HARRY W. LYMAN: I will not take any time in complimenting Dr. Grove. It seems to me that it is an unfortunate thing that Ménière's name has been hooked so firmly to this symptom of vertigo. Of course there is the triad, deafness, tinnitus and vertigo, but many people, when they see a case of vertigo, immediately say—"Ménière's synrome or pseudo-Ménière's syndrome" and think they have made a diagnosis. It has been brought out this morning that there are probably a number of different underlying causes for the disturbance in hearing. I think the most striking one has been the allergic condition. As Dr. Grove mentioned, the symptoms can be brought on by administering the offending agent. The same symptoms occur with an eighth nerve or pontine angle tumor, and on superficial observation one might not distinguish one from the other. Other cases we see are due to intoxication of the labyrinth. Then I recall one patient who was sent in with a diagnosis of Ménière's disease, in whom it transpired that the deafness was of 18 years' standing and due to mumps; the vertigo and tinnitus were of only one year's duration. So I think we must get away from the idea that we are dealing with a single disease. There are a number of underlying causes, and we must try to discover their origin. As to surgical interference, I think most otologists agree it should be a last resort. Of course, in many cases the disease is so disabling that the patient is willing and anxious to submit to any operation that relieves the vertigo. Operation does relieve him and he does not mind the deafness, but it should not be done in cases in which attacks are brought on by such things as eating chocolate.

DR. MILLARD F. ARBUCKLE: I have heard emphasis laid on what is called "horse sense"; the use of "horse sense" is essential in the study of these patients. I have found it very helpful to have them studied by a good internist from the standpoint of disease of the circulatory system or of the endocrine system. I have seen quite a few cases with complaints as mentioned in which disorder of the thyroid gland, particularly hypothyroidism, was present, and in which the symptoms were relieved by the administration of thyroid gland. I have had one experience with a celebrated physician who woke up one morning so dizzy he could not get out of bed, and for a week was wholly disabled. Finally after two weeks or so he made a complete recovery after taking Vitamin B and with no other treatment.

DR. THOMAS GALLOWAY: I would like to ask Dr. Grove if he used thiamin chloride intravenously.

DR. WILLIAM E. GROVE (closing): This paper was in the nature of an evaluation and not the result of personal experience with this condition, and there is not much to add except to thank the discussors. In reply to Dr. Galloway, I have not used thiamin chloride, but I would like to say something more about histamine. In the paper due credit is given Drs. Sheldon and Horton for their work with this agent. I have had considerable success with it, particularly in the acute period of vertigo, and as Dr. Shea said, the drug should be given intravenously and very slowly. I have used the amount originally prescribed by Sheldon and Horton, 1.9 mg. dissolved in 250 cc. of normal salt solution and injected over a period of one and one-half to two hours, and I have also had some experience with the follow-up treatment in which the drug is given subcutaneously in smaller doses two or three times a week. Heartened a little by the work of Sheldon and Horton, and feeling as I do that some of the headache and dizziness which comes on in spells after a head injury is possibly and probably due to vasomotor disturbance at that particular time, I have made use of the drug in that particular type of case and have had some success. The success has not been apparent in every case, but in some the results were rather dramatic.

Complications of Esophageal Perforations

PAUL H. HOLINGER

(Abstract)

A brief review of the anatomy of the esophagus and the surrounding structures is presented, and the etiology of esophageal perforations and their complications is discussed.

The complications of esophageal perforations are:

a. Infections; periesophagitis and abscess.
b. Hemorrhage.
c. Perforations of the pleura.
d. Emphysema.
e. Pericarditis.
f. Perforations of the trachea and bronchi.

The diagnosis and treatment of these complications are discussed, and representative cases are presented.

DISCUSSION

DR. SAMUEL J. PEARLMAN: I find myself very much in the position of Dr. Brunner—this paper is remarkably complete and I cannot add anything to it. I find myself in agreement with the essayist, so we cannot give you the spectacle of a lively debate. It would not be possible, of course, to cover the entire paper and take up the various details. I would like, if I may, to throw some light on this subject by discussing my own fears and anxieties in situations of this character and limiting the discussion to the narrow aspect that concerns us most closely as laryngologists, leaving the difficulties that occur in the chest to chest surgeons.

A review of the literature shows that the chest surgeon is inclined to be surgically minded when the difficulty is in the neck, advising the laryngologist to go in and not hesitating to go in himself; but he displays a laudable caution when the trouble is in the chest. Without casting aspersions, is it possible that the surgical attitude here is influenced chiefly not by the danger of the disease process, but by the technical difficulties of the approach?

Now, as to perforations high in the neck; I do not know how you are affected by them, but for my part I am always anxious. Given a foreign body that may or may not have perforated, how can you tell? If you have removed it, have you done any damage

in removing it? If you avoid interference and the patient develops a rapidly developing mediastinitis, your conscience plagues you. You say to yourself, had I gone in early, this might not have happened. On the other hand, if you want to intervene and the patient refuses, and a colleague bolsters him up in his refusal, and he develops nothing, or perhaps a localized periesophageal abscess which evacuates itself spontaneously—you are in the position of having advocated something that was not necessary for a condition which cured itself.

In the literature there are any number of astounding cases reported with a great deal of trauma to the esophagus, and still the patients recover without external intervention. I remember one case Dr. Iglauer wrote of and another reported from the Mayo Clinic in which a lead toy soldier went through the esophagus and into the mediastinum. This was removed by esophagoscopy and a complete recovery ensued. I remember in my own experience a patient who swallowed a chicken bone, which disappeared after a probang had been used. The bone disappeared, but the patient's discomfort continued. Upon esophagoscopy nothing could be seen at first. I was prepared to quit when a white spot showed itself, the size of a match head, just below the pinch cock. I seized it with a forceps and out came a bone as long as a match. That patient made a complete recovery with an infected foreign body outside and parallel to his esophagus for several days. I do not know the complete answer to this type of case. It is difficult to get a clear answer from the literature. It does seem that there is a little more tendency recently to wait awhile. This does not mean that surgical intervention has not its proper time and place. It is obvious, however, that there can be no absolute rules to follow, much as we would like to have such rules. Our guide is the best of skill and judgment we can muster with the knowledge that all our experience may not avail.

Dr. Samuel Iglauer: Dr. Holinger has raised a very important question, namely, when to operate. There is no argument about the cause of these things, and there is very little additional to be said about diagnosis, except that X-ray will often enable one to make a diagnosis of perforation before it can be made by any other method; i. e., roentgenograms taken early will often show gas bubbles about the foreign body where there is no palpable emphysema in the neck. One knows from the roentgenogram that one is dealing with perforation. Where one suspects perforation and wants to use the X-ray I think it is better to use lipiodol rather than barium because if there is any leakage or the trachea is involved, lipiodol is less irritating.

Dr. Pearlman has raised the same question about when to operate. That reminds me of the early days of appendicitis, when it was the practice to give morphine and wait. That is not done now. The surgeon makes the diagnosis and takes out the appendix or takes it out even before he makes the diagnosis. As for the policy of watchful waiting—what are we waiting for? We are waiting to see whether the patient is going to get better or get worse. The longer we wait, the worse he gets, and the longer we wait, the less chance for success. The surgical approach in the neck is not difficult. Suppose one gets down to the esophagus—if there is no pus, one has done no particular harm. On the other hand if the patient develops a spreading mediastinitis or pleurisy it may be too late. Therefore, I think it is better to take a chance on operation rather than to delay. I think Dr. Holinger did a clever thing when he approached the foreign body through the neck, and then instead of pulling it out, pushed it back into the esophagoscope.

I do not blame the thoracic surgeon for being timid about posterior mediastinotomy. If he ruptures the pleura, he gets complications. On the whole, I should say he would be much safer in operating than in waiting.

Dr. Millard F. Arbuckle: I have been delighted with Dr. Holinger's presentation and with the discussion of this very important subject. Dr. Holinger's opening gun was that these cases are "notorious for the amount of trouble they cause," and I think we will all agree with that statement. Before I forget it, Dr. Iglauer mentioned gas bubbles. We must remember that very often we have a gas bacillus infection which is deadly under the best of conditions.

In deciding upon treatment for esophageal injury we must consider the nature and extent of the injury. It is well recognized that such injuries may range from slight laceration (as is almost certainly true in every foreign body case) to more severe injury such as a small puncture wound, or to still more severe injury such as extensive tear or rupture of the esophagus with pneumothorax, etc. Cases of the first group usually get well merely with rest of the esophagus. Those of the second group in many instances get well with similar treatment, but I am always more apprehensive about them for the succeeding day or two until I am sure they do not show signs of developing mediastinitis. Chemotherapy is an important part of their treatment, I think, as a prophylactic measure at least. In the third group, in which we are sure of tear or rupture of the esophagus, immediate drainage of the mediastinum is indicated, if in the upper

mediastinum, cervical drainage, and if low down along the course of the esophagus, drainage by the posterior route.

We feel very strongly that "watchful waiting" for the development of proof of mediastinitis or abscess formation deprives the patient with this extensive type of injury of his best chance for recovery.

Dr. Thomas Galloway: I rise to record my vote in favor of interference after perforation. I was surprised to hear Dr. Holinger say that most men believe that one should wait—it was my impression that it was quite otherwise. In the first place, when one goes down only to the esophagus, in the absence of infection one does no harm. In work on the upper esophagus in the dog, when I put in a preliminary pack, there was no descending infection, and one could do almost anything afterward in that area. I should think in any case in which one is certain of perforation in a region which is accessible through the neck, one should open to the perforation and pack it off with external drainage.

The operation of cervical mediastinotomy, in a clean field, has little element of danger; perforation with infection without external drainage offers the major odds against recovery.

Dr. Paul H. Holinger (closing): This discussion has certainly been stimulating. I believe I must first clarify a point which is covered fully in the paper but because of the limited time could be covered only hastily. I agree that immediate mediastinotomy is indicated in cases of mediastinitis and extending periesophageal suppuration. My mention of conservatism dealt with patients in whom the diagnosis of esophageal perforation was still somewhat in doubt in spite of a low-grade temperature or even, occasionally, cervical emphysema. This type of case is variously described in the literature, and most authors indicate that the patients recover in the course of a few days without surgical interference. Head, Myerson, Von Eycken, Clerf, and others stress the conservative management of this group of cases.

Careful, watchful waiting means, of course, frequent temperature readings as well as repeated white blood counts. I thoroughly agree that any increase in findings indicates immediate surgery. Dr. Pearlman mentioned laceration of the esophagus as opposed to perforation, and this difficult differential diagnosis is all important. Routine mediastinotomies in questionable cases would appear to be unnecessary, and I cannot agree with Dr. Galloway that such an operation is simple and without danger.

This brings us back to the question of the term "prophylactic mediastinotomy." This term originally denoted drainage of the mediastinum through the neck in cases of external trauma to the esophagus, such as occurred from stab and gunshot wounds. At the present time, the term is frequently used loosely to designate the opening of the retropharyngeal space and the placement of a gauze pack in the inferior part of the wound in an attempt to keep the infection from traveling into the mediastinum. Dr. Lederer and Dr. Fishman suggested clarification of this term in an article written in 1934, and gave reasons for and against the operation. Certainly the term should not be used when a simple mediastinotomy is done to drain an advancing mediastinal infection due to an esophageal perforation.

CHICAGO LARYNGOLOGICAL AND OTOLOGICAL SOCIETY

Meeting of Monday, November 4, 1940

THE PRESIDENT, DR. ROBERT H. GOOD, IN THE CHAIR

Labyrinthitis and Meningitis with Recovery: Case Report

WILLIAM E. GROVE

AND

GERHARD D. STRAUS

(This paper was printed in full in the ANNALS, 50:288 (March) 1941)

DISCUSSION

DR. W. E. GROVE: I once heard an otologist ask the question, "How can you tell when a serous labyrinthitis becomes purulent?" The answer was, "I do not know," and I have to confess that this is also my position. We do not know whether this was a serous labyrinthitis which had become purulent. Certainly the labyrinth was not dead, although we could not get any response to cochlear stimulation. The child was too sick to perform many labyrinthine tests, and we do not know whether vestibular function was out at that time. We made as thorough a search as possible for a pathway into the meninges and were unable to find any lead anywhere. Because there were very definite labyrinthine signs we felt that the infection traveled through the labyrinth into the meninges and produced a meningitis.

We are frank to say we do not understand a number of things about this case, but we think it interesting that under the chemotherapeutic attack the cochlear function, which to the best of our knowledge was gone completely, returned to a considerable degree

as shown on the audiogram. This brings up the question as to whether past ideas about labyrinthine surgery must be changed somewhat in the light of the modern use of chemotherapeutic drugs.

DR. ALFRED LEWY: Another has been added to the growing list of meningitis cases successfully managed by modern chemotherapy. I should say this case could not be classified as labyrinthogenous meningitis. The Weber was referred to the operated ear, which indicates that there was some function in that labyrinth, and, subsequently, the return of a certain degree of hearing further indicates that this was in all probability a serous and not a suppurative labyrinthitis. Failure to find a direct avenue of connection with the meninges occurs very frequently in mastoid surgery even where there is no question as to involvement of the labyrinth, so the absence of such avenue gives us no real information.

I think the great question is brought out by Dr. Grove, as to how far chemotherapy is going to supplant surgery in otogenic meningitis. Before the days of sulfanilamide we never expected our hemolytic streptococcus cases to recover and very few did, either with or without surgery. In other words, we never saw surgery do any particular good in otogenic meningitis. Now it is a usual occurrence for such cases to recover under chemotherapy. The question as to whether the labyrinth should be operated upon I believe should be extended as to whether the mastoid should be operated upon. Personally I know of several cases of otogenic meningitis in which the meningitis was produced by unquestioned otitis media and no other cause was found, and yet these cases recovered without surgery. I am not decrying surgery if there is any definite evidence of breakdown of the mastoid or if the case has gone on for two or three weeks, even though breaking down of the bone cannot be diagnosed. It is probable here that extension is taking place through the mastoid, and I believe that in such a case surgery is indicated. I know of one case in which the period between the first symptoms of otitis media and the onset of meningitis was nine days, and that case recovered without surgery.

We are, therefore, not yet prepared to answer that question. We have not had enough cases in which we determined not to operate, but I believe the question will require an answer sooner or later.

DR. FRANCIS LEDERER: Many things that are interesting at the time to the person who observes a case are lost when it is reported

later. I believe it was said that "most surgeons report the cure of labyrinthitis by labyrinthectomy." I believe that statement covers too much ground. I do not think labyrinthine operations are done on all cases that show a nystagmus; at least that is not our policy. There is one factor to be borne in mind in this case. This was a young child, and prognostically children offer a better outlook in meningitis than do adults. Also it is possible that you were dealing with a circumscribed type of meningitis near the cisterna, and these often remain circumscribed for a long time. I understood that the Weber was lateralized to the affected ear and other functional tests were not done. There is therefore much about the case that remains rather vague.

The past history of the case and the findings of granulations as described might bring up two thoughts, namely, that this was a Streptococcus mucosus type of infection or that it was an acute exacerbation of a chronic suppuration. The thought also occurred to me—was not this really a middle ear process and were indications really present for a radical mastoidectomy? It is possible that an attico-antrotomy would have sufficed, and in view of the priority for the successful outcome which has been given to sulfanilamide, is it not possible that the operation deserves credit for the result? The sulfanilamide was given postoperatively, and it is very difficult to say that a case with 3900 cells in the spinal fluid would not have recovered with an attico-antrotomy or a radical mastoidectomy. I believe that otologists particularly have to guard against reporting cases and giving direct credit to the drug for the results obtained, rather than admit that a focus has been eradicated and proper drainage established, and that therefore the operation had something to do with the recovery.

Dr. Thomas C. Galloway: I like this definition of serous labyrinthitis; if the function of the labyrinth is restored, the patient had a serous labyrinthitis, if not, it was suppurative. I understood from the report that only one hearing test was made. This may be an important point of differentiation and should be repeated frequently.

Two weeks ago I had a patient with a pneumococcic ear, marked dizziness, nystagmus to the opposite side and a non-reactive labyrinth. For four days there was no hearing with the opposite ear masked, but on the fifth day the spoken voice could be heard at one foot. A complete simple mastoidectomy was done, sulfapyridine was given, and the patient has rapidly improved. If one makes hear-

ing tests often, usually in serous labyrinthitis at some time the cochlear function will be found present.

One question that may be important is how far, if at all, can invasion of the membranous labyrinth go with resolution? A French author about two years ago attempted to show by histologic studies that recovery could occur in a slow process even where there was invasion.

Dr. W. E. Grove (closing): Dr. Lewy's statements with reference to the question of operating or not operating on these cases interests me very much, but in spite of the decided benefit of chemotherapy I do not believe I would have the courage to withhold operation in this type of case. In spite of the best methods of examination at our disposal, I do not feel that I know definitely whether there was actual bone pathology in this case. It was a clinic case, and as usual there was considerable difficulty in getting an accurate history. As Dr. Lewy said, granulations were within the tympanum, possibly indicating chronicity, but I do not think I would have the courage not to operate as widely as possible, and therefore a radical operation was done.

Dr. Lederer questioned whether the cure came from the operation or from chemotherapy. I do not know. I think possibly it came from both, but as Dr. Lewy said, prior to the use of chemotherapy the cure of these cases was extremely rare, and for that reason I would attribute the cure more to chemotherapy than to our operative interference. I do not believe this meningitis was a localized affair, because if it were I would not expect to get a culture of hemolytic streptococcus in the spinal fluid removed by lumbar puncture. I think with Dr. Galloway that this probably was a serous labyrinthitis. I did not state that it was a purulent labyrinthitis, although I did state that in our opinion the infection went through the labyrinth to reach the meninges because we were not able to find any other source of infection. I do admit that our methods of treating infections through operative procedures are not so effective but that we might have missed a lead. How much infection of the labyrinth can be present and recovery still take place I do not know. We cannot always be sure that there has been a purulent invasion of the labyrinth. We cannot always be sure when we say we have a serous labyrinthitis that we have not had a purulent infection that has been taken care of. It is assumed that if a labyrinth recovers function there has been a serous labyrinthitis and not a bacterial invasion. I do not know that that question has ever been absolutely solved.

Chemotherapy in the Treatment of Complications of Acute Middle Ear Suppuration

JOHN R. LINDSAY

(This paper was printed in full in the ANNALS, 50:159 (March) 1941.)

DISCUSSION

DR. GEORGE LIVINGSTON: After such a thorough dissertation there is little to discuss of the individual features of any case. I would like to supplement Dr. Lindsay's experience with additional cases from Children's Memorial Hospital, which may have some bearing in so far as statistical material is of value. The value is limited, because the number of cases is still not large enough to enable us to draw final conclusions from the standpoint of the effectiveness of chemotherapy in early otitis media. There is no question of its value in the serious intracranial complications.

With a view to estimating its value before complications have occurred, we collected a series of early cases in the outpatient department, from January to June, 1940. This differs from a series of hospital cases, which may come in with complications. This series was divided into approximately equal parts. Of 332 cases, 178 had chemotherapy; the hemolytic streptococcic cases got sulfanilamide, the pneumococcic cases got sulfapyridine; 154 cases were treated without chemotherapy. The figures are not impressive and the differences between the two groups is not great; nevertheless it may be of significance if the treatment is carried out in various other clinics and the results uphold these findings. The duration of otitis media in the cases untreated by chemotherapy was 19.5 days and in the treated cases was 14.5 days. The number of mastoid complications that occurred was 7.8% (12 cases) in those treated symptomatically, 2.8% (5 cases) in those treated by chemotherapy.

These figures do tend to favor the action of sulfanilamide in early cases. On the other hand in hospital cases, many of which came with frank mastoiditis, the majority had not had sulfanilamide, but some did have and are included in the outpatient group. In 1939, 91 mastoid operations were done, of which 19 had received adequate chemotherapy. This does not prove anything except that mastoiditis can and in some cases does develop in spite of chemotherapy. In 1940, for ten months, in 112 mastoid operations 35 cases had adequate chemotherapy, approximately the same percentage.

If one is to engage to give sulfanilamide or sulfapyridine in the early stages, adequate doses should be given immediately in severe cases. We have found some which responded favorably; others did not. If there is no response in three days we stop it entirely. If there is a response we have an additional problem because we know that to stop medication before the disease is completely cured may lead to a recrudescence and leave the patient in a more precarious condition. I would like to emphasize one feature in the use of this drug. The leucocyte count usually drops. There are two significant drops in our experience. Usually the leucocyte count falls rapidly to normal and remains there. We have found a few cases in which the count reached normal level and then continued to drop. Once committed to chemotherapy we have to stay with it until the temperature is normal, the ear is dry and the patient is entirely well. The count may continue to fall even as low as 1,500 with marked diminution in granulocytes. Sometimes in ten or twelve days when signs of mastoiditis appear the patient has a low leucocyte count and is less able to combat infection. That is not an argument against chemotherapy, but it is a factor that must be considered. We are inclined, if a case shows signs of complications, to operate somewhat earlier in those treated with chemotherapy than in the others. We feel less confident in letting the case go on because we cannot evaluate the clinical picture as well.

Dr. Meyer S. Fox: Dr. Lindsay and Dr. Livingston have covered the subject of chemotherapy in meningitis and otitis media. I wish to present an additional case of acute otitic meningitis which showed some interesting clinical problems.

The chart illustrating the clinical course is self-explanatory. This child, six years of age, weighing 60 pounds, was admitted to the hospital with bilateral otitis media, the ear drums having ruptured spontaneously and drained for one week. He was placed on neoprontosil, 45 grains daily, and this dose was continued for six days, at which time the clinical course showed decided improvement and the right ear had become dry. The drug was discontinued, and after three days he was about to be discharged when he developed headache, vomiting, and subsequent signs of meningitis. The temperature was 104.4 degrees, spinal puncture showed 2,000 cells, 95% of which were polymorphonuclears, and direct smear and culture of the fluid were positive for hemolytic streptococci. A simple mastoidectomy was performed on the left side and chemotherapy started. He was given 60 grains of sulfanilamide orally daily for four days; with improvement in clinical symptoms this was

reduced to 45 grains daily. The blood concentration was 5.6 mg. The spinal fluid and clinical course continued to improve, and after one week the sulfanilamide was reduced to 30 grains daily. Fifteen days after the original onset of the meningitis there was an abrupt recurrence of the meningitic picture and spinal fluid findings, the cell count rising to 1775. The mastoid wound was explored, but there were no significant findings.

It was felt that the activation was due to the drop in the sulfanilamide dosage. We therefore increased the intake to 60 grains of sulfanilamide and 60 grains of neoprontosil daily, which resulted in a blood level of 8.5 mg. He was carried on this dosage for twelve days, and it was then reduced gradually during the next four weeks, during which the clinical course and spinal fluid findings gradually improved. There were several periods of definite temperature elevation. Supportive measures were used, and during the hospital stay it was necessary to give 11 transfusions, varying between 250 and 300 cc., in order to keep the blood hemoglobin up to 12 grams.

This case shows the tendency for remission and exacerbation of meningitic symptoms which occur when the sulfanilamide dosage is stopped or cut rather abruptly, the necessity for giving adequate amounts of the drug in order to control the clinical picture, and the depressing effect of the drug upon the blood hemoglobin.

CHICAGO LARYNGOLOGICAL AND OTOLOGICAL SOCIETY

Meeting of Monday, December 2, 1940

THE PRESIDENT, DR. ROBERT H. GOOD, IN THE CHAIR

Otosclerosis in Identical Twins

ELMER W. HAGENS

(Author's Abstract)

Very few reports of this condition have appeared in the literature. The history of the case reveals that the mother of the twins has had progressive deafness since the age of 17 and that following the birth of the twins the hearing became noticeably worse. Examination of the mother shows definite otosclerosis. She was one of ten children, and there has been deafness in all but two of them, beginning in childhood in the majority.

The identical twins are girls aged 24. The hospital record states the placenta was single, larger than normal, with lateral cord insertions and thin membranes. The girls grew up together, looked alike and were difficult to tell apart, had like schooling, environment and illnesses. Neither ever had discharging ears. Both have had frequent colds, and teeth that crumbled. They disliked fresh fruits and vegetables, while eating considerably of starches and sugars. These points are brought out for what they may be worth. At the age of 17 one of the twins, Florence, began to notice difficulty in hearing, while her sister noted the same thing some time later. However, Florence married at the age of 17 and, one year later at the birth of a child, her hearing became much worse and has remained definitely below that of her sister to the present time. Discounting the time difference in onset of deafness, Florence's hearing is worse than her sister's, and the bearing of a child appears to be the only factor wherein the sisters have not been alike.

DISCUSSION

DR. GEORGE E. SHAMBAUGH, JR.: Identical twins develop from a single ovum so that presumably all inherited factors are shared equally. It would seem that otosclerosis in identical twins offers the ideal opportunity for determining the importance of heredity compared to external factors in this mysterious disease. However, there may be one complicating factor in the situation. It is said that identical twins are no more alike than the left and right side of an individual, since one twin develops from the right half of the ovum at its first division and represents the right half of the individual originally intended, while the other twin represents the left half. Deafness in otosclerosis is not always symmetrical but frequently develops earlier or more rapidly in one ear. Nager finds that the deafness is confined to one ear in 10 per cent of cases. Therefore when one identical twin develops clinical otosclerosis sooner than the other it may only mean that the individual originally intended would have become deaf in one ear first.

Considering this complicating factor it is remarkable how otosclerosis runs a similar course in all the identical twins thus far reported. Dr. Hagens' report represents a valuable addition to the five cases previously reported. It suggests but does not prove the importance of pregnancy as an accelerating factor in the deafness of otosclerosis. The importance of pregnancy in otosclerosis has probably been exaggerated. In my own experience there is only a one-in-five chance of a further loss from pregnancy while Nager finds the chances to be one in 4.8. More cases like Dr. Hagens' will help to prove the importance of pregnancy and perhaps of other predisposing factors on the deafness of otosclerosis.

DR. ALFRED LEWY: Are there any cases on record of unilateral deafness in identical twins?

DR. SAMUEL SALINGER: I would like to ask if in these cases the basal metabolic rate was determined, or whether the blood calcium determination was made? Such data might or might not be of value as corroborative evidence in evaluating the differences in the hearing ranges.

DR. ELMER W. HAGENS (closing): In answer to Dr. Lewy, I believe all cases are bilateral. In reply to Dr. Salinger, I did not ascertain the basal metabolism on these girls, because soon after I examined them one moved away and has just recently returned, and I have not had it done. However, it has been mentioned as one of the findings in these cases.

Anesthesia in Otolaryngology

STUART C. CULLEN

(Author's Abstract)

An attempt will be made to show how a knowledge of certain fundamentals in anesthesia such as the use of proper preanesthetic medication, an adequate airway, and sufficient oxygen supply can increase the convenience to the surgeon and the comfort of the patient, and minimize the hazard to the patient. Individualization of each patient relative to the anesthetic agent and technic to be employed is an indispensible accompaniment of good anesthesia.

Drugs used for premedication have several functions, all of which influence only the anesthesia; the surgery is influenced only indirectly by the premedication in so far as it aids or hinders the anesthesia. As a consequence, the drug selected, the amount used and the time it is given should be determined with reference to the anesthetic agent and technic employed.

The three functions of preanesthetic medication are the allaying of apprehension, heightening of the pain threshold with lowering of metabolic activity, and certain specific functions such as the drying of secretions.

Of the drugs commonly used, morphine is the most efficient, producing the greatest depression of reflex irritability, analgesia, and reduction of metabolism with the least interference with normal protective mechanisms. The maximum action of the morphine should be obtained before anesthesia is instituted. If not, the benefits to be derived from it are minimal, difficulty with the induction and maintenance of anesthesia is frequent, and prolonged severe depression supervenes postoperatively. When given subcutaneously, morphine reaches peak effect in 60-90 minutes, given intramuscularly it reaches maximum effect in 30-45 minutes and when given intravenously the total action occurs in 10-20 minutes. The same dosage may be used for all three routes. When given intravenously, morphine should be diluted with approximately 5 cc. of saline or water and given slowly over a period of 2-3 minutes.

Scopolamine and atropine have two functions in common: (1) The prevention of secretion and (2) the reduction or elimination of certain vagally mediated reflexes. In addition to these functions scopolamine produces marked psychic sedation and amnesia and is to be preferred for premedication over atropine.

The barbiturates have two functions: (1) Hypnosis and (2) protection against the convulsive manifestations of a cocaine or similar drug reaction. The short acting barbiturates, whose maximum effect when given by mouth is obtained in 20-30 minutes, are preferred and when given in combination with morphine and scopolamine should be given one-half hour before those drugs.

Morphine and scopolamine are used in the ratio of 25 parts of morphine to one part of scopolamine. This combination produces a minimum of respiratory depression and nausea and emesis, with a maximum of benefit. The dosage is dependent upon a number of factors influencing the metabolic activity of the patient.

The use of routine doses of the drugs mentioned can only result in a large proportion of unsatisfactory anesthesia. The scientifically individualized use of these drugs can make the difference between a successful operation and an unsuccessful one, particularly under regional, topical or infiltration anesthetic technics.

The establishment and maintenance of an adequate airway is a prime consideration in any anesthesia and is particularly significant in otolaryngologic anesthesia where the surgery is about the upper respiratory passages.

The most important contribution to the maintenance of an airway during anesthesia is the employment of an endotracheal technic. This assures a patent airway in all positions, facilitates removal of the anesthetist from the field, prevents aspiration of blood or mucus, allows for suction and cleansing out of trachea and bronchi, reduces amount and concentration of agent necessary and permits manipulation about and full vision of face and pharynx without interfering with the anesthesia.

The difference between good anesthesia and poor anesthesia is usually the difference between a good airway and a poor airway. All too frequently the death of a patient under anesthesia can be ascribed to an inadequate airway.

Regional, infiltration and topical methods of anesthesia in otolaryngology are most conveniently performed by the surgeon. The anesthesiologist's principal interest in these forms of anesthesia is in the premedication and treatment of reactions.

Other methods of anesthesia are inhalation, rectal and intravenous. Inhalation anesthesia has several advantages in that minute to minute control is possible, there is no time limit, it is available to practically all patients, and the co-operation of the patient is not

needed. Disadvantages are that there is sometimes a delayed return of reflexes and explosive potent agents must be used on occasion. The rectal technic has advantages in that the induction is pleasant and the agent is nonexplosive. Disadvantages are that there are respiratory and circulatory depression, slow return of reflexes, frequent supplementing with other agents, imperfect co-operation, no control, and increased laryngeal reflexes. Intravenous barbiturate anesthesia is advantageous in that the induction and recovery are quick and pleasant, the agent is non-explosive, there is no irritation of respiratory mucosa, and relaxation is complete. There is, however, no control of this drug, respiratory and circulatory depression, increased laryngeal reflexes, and two persons are necessary for proper administration.

It should be emphasized that, contrary to popular opinion, control of the airway is as important in rectal or intravenous technics as in inhalation technics. Merely because the drugs are administered by routes other than the upper respiratory passages does not mean that the establishment and maintenance of an airway is not important. Most of the difficulty arising from the use of these technics is due to improper control of the airway.

In conclusion, it is evident that many anesthetic agents and technics are available for otolaryngologic work. It should also be evident that the agents and technics in themselves are of little value unless utilized by a person capable of selecting and maintaining the anesthesia best suited to each occasion. This capability is most frequently obtained in a physician able to apply physiologic fundamentals.

DISCUSSION

DR. THOMAS C. GALLOWAY: I am favorably impressed by Dr. Cullen's extensive premedication. Recently I have been using more premedication, almost to the point of basal anesthesia, and find that operations not previously satisfactory under regional anesthesia are remarkably so with more premedication, and I have been rather weaned away from avertin. One should emphasize the care of the patient while getting the effect of premedication. At one hospital we have to give morphine and scopolamine while the patient is in a noisy ward and has to walk a distance to the operating room, and the results are unhappy. The patients are likely to be tense and resistive. In another hospital the head nurse does not let anyone go into the patient's room while the premedication is taking effect and even puts cotton into the ears to avoid noise, and these patients are

relaxed and cooperative. I am glad he emphasized certain dangers that may occur with intravenous anesthesia. It is one thing to administer such anesthesia when there is very close supervision with appreciation of the dangers, and another when it is casually given by an untrained interne. In a relatively small number of cases I know of two fatalities. I think it is something that appeals to us; it is out of the way of the field of operation and is very simple, but I think it could be over used.

Another question is the use of premedication with the abolition of the cough reflex. We must not lose sight of the fact that this cough reflex is most valuable in preventing pneumonia or atelectasis. Jackson emphasizes that in many cases of bronchoscopy one should not use opiates.

I should like to have him tell us what anesthesia he chooses for surgical diathermy around the head; I have used with satisfaction both avertin and intratracheal nitrous oxide. Is there any hazard of explosion with the latter?

Dr. William H. Cassels: First I would like to express my appreciation of the opportunity of discussing Dr. Cullen's excellent and comprehensive paper. There are few specialists who recognize the difficulties the anesthetist has, and I think the otolaryngologist is one of the few who do. He is accustomed to think of the upper respiratory tract, as is the anesthetist.

Dr. Cullen emphasized the advantage of a free airway and the advantage of endotracheal anesthesia in certain cases. I have seen several cases recently which brought out one advantage in having the endotracheal apparatus, that is the facility with which we can deal with an emergency if it arises. I have in mind two cases in which there was respiratory arrest, probably due to neurologic complications. In one case a cerebellar abscess resulted in respiratory arrest during mastoidectomy; in another case an operation was being performed for a retropharyngeal abscess. Respiration ceased during operation and returned spontaneously only after completion of the operation. This was probably related to pressure on the carotid sinus. In each instance the endotracheal technic made it easy to control respiration and avoid complications.

I would like to offer a few constructive criticisms. In no type of work is it more difficult to put a patient to sleep than where a surgeon has tried and failed to do an operation under local. The operation has been started in a region the anesthetist would like to

get at, the patient is stimulated by the local anesthetic drug, he may be suffering pain, and he is psychologically disturbed, which makes it difficult to produce good anesthesia. In such cases the hazard for the patient is greater than the hazard of both types of anesthesia separately. Patients are subject to hazards in both local and general, and this is enhanced by the difficulty of inducing anesthesia under these circumstances.

Dr. Cullen mentioned the hazards of ventricular fibrillation under general anesthesia. There are two circumstances which are likely to cause this in your work. No surgeon is more addicted to the use of adrenalin than the otolaryngologist, and when adrenalin is used in packs in the nose or in a wound, some is absorbed and is apt to cause ventricular fibrillation under general anesthesia. Another circumstance is the attempt to carry out minor surgery under very light anesthesia. We know this is true of chloroform and probably ethyl chloride also. In cases such as myringotomy it is tempting to use some potent, quickly acting agent. As soon as the patient is quiet the surgeon incises the ear drum, which stimulates the patient, perhaps the adrenals are stimulated, and ventricular fibrillation and death may occur. Even minor procedures should be regarded as hazards under general anesthesia, and as much care should be taken as in more elaborate procedures.

I was impressed with Dr. Cullen's mention of intravenous anesthesia. We have used it frequently, and our experience in several cases has made us wonder whether it is advisable. In a very simple operation to remove a polyp from the ear, we thought we would inject a little pentothal, and the patient started to cough and persisted in coughing until after the operation was completed, and nothing we could do would stop it. One great hazard is the temptation to add more anesthetic agent, and the danger is that we will stop respiration before we stop coughing and spasm.

Dr. Nora B. Brandenburg: I am interested in this subject as an anesthetist, and it brings basal anesthesia to the attention of every otolaryngologist. Basal anesthesia is a state of unconsciousness produced by such drugs as nembutal and other barbiturates so commonly used in the office, and it behooves us all to know their action and the signs of an overdose.

I am also interested in the action of these drugs on the mucous membranes. Recently I observed nembutal in overdose, and noted an increase in secretion from the mucous membranes of the tracheobronchial tree and the vaginal mucosa. The barbiturates produce

edema of the lungs, and aspiration pneumonia is the most serious complication. From my observation, certain of the popular vitamin products with nicotinic acid produce, even in small doses, similar reactions in sensitive individuals. This allergic response may account for the coughing in some of the barbiturate anesthesias mentioned by the speaker. Anesthesia is a specialty and should be recognized as such by all branches in medicine.

DR. B. B. LENNON: Dr. Cullen made mention of the deleterious effects of divinyl ether upon the liver and that is quite true in prolonged anesthesia. However, where vinethene is used for only five to ten minutes of anesthesia, no contraindications are found. Vinethene has not an unpleasant odor, and both children and adults after several breaths may be brought to a very pleasant degree of analgesia from which they recover smiling in many instances, with a memory of having had a pleasant dream. It has been a common experience at Michael Reese Hospital to have a child come into the operating room crying and fearful, and to go out smiling. Patients go to sleep and awaken in a few seconds.

We have found endotracheal anesthesia to be of particular importance in that type of adult patient who has been booked for a tonsillectomy under local anesthesia, and who refuses at the last moment to go through with it. Here endotracheal anesthesia serves a worthwhile purpose. The comparison between the behavior of an adult under the ordinary method of open-drop or insufflation and endotracheal technics leads one to believe that the latter offers security and peace of mind to both surgeon and anesthetist, and protection of proper oxygenation to the patient out of all proportion to the added complexity or expense of the technic.

Where diathermy is contemplated in the upper respiratory tract, it is our policy to cocainize the pharynx and larynx as though for a bronchoscopy, set up an intravenous infusion of normal saline, inject a small amount of pentothal sodium, introduce a nasal endotracheal or oral endotracheal tube (depending on the location of the pathology) and then maintain the patient adequately with at least 20 per cent oxygen, under nitrous oxide. All these patients must be seen by the anesthetist prior to operation, and given a premedication of either gr. 1/6 morphine sulphate and 1/150 scopolamine, or morphine sulfate gr. 1/25 and 1/100 scopolamine in single or double dosage, depending upon the age and debility of the patient.

Endotracheal technic in the hands of the expert will not result in harm to the larynx or other structures. Some surgeons fear that

a tube in the respiratory tract will produce damage. I should like to cite a few cases to the contrary: The late Dr. Sonnenschein had an endotracheal tube in position almost constantly during the last four days of his illness, which was used as an airway to allow ingress of oxygen and the removal of secretions to prevent him from drowning in his own respiratory debris. Postmortem examination showed no deleterious effects. Recently an endotracheal tube was kept for 55 hours in a young girl, and postmortem findings revealed nothing abnormal in her respiratory tract. While Dr. Cullen and I were at Bellevue Hospital, we had an opportunity to observe a patient who had an endotracheal tube in position continuously for approximately 176 hours and who died about 36 hours after its removal, from metastatic abscess of the lung and hemorrhage. However, it was the opinion of the department that the tube had not affected the upper respiratory tract.

Some men object to the endotracheal tube, yet not to the bronchoscopic tube. I believe we all realize that in expert hands, endotracheal tubes and anesthesia can be nothing but a boon to everyone.

Dr. J. Allen Weiss: I should like to ask Dr. Cullen to comment on the additional hazard presented by intensive sulfanilamide therapy in general anesthesia, and what precautions he uses in the management of patients operated on at the time of high sulfanilamide blood concentration.

Dr. Howard C. Ballenger: For a year or so I used the scopolamine-morphine combination as a preoperative preparation for local anesthesia. I had three or four instances of marked respiratory depression which I attributed to the scopolamine as I have not had this mishap following the use of morphine and atropine. Perhaps my prejudice against scopolamine is unjustified. I would like to have Dr. Cullen comment on this.

Dr. G. H. Mundt: For many years I have noted several things which are apparently not sufficiently appreciated by either the hospital personnel or by the surgeon. One is that in the preparation of a patient for an ear, nose or throat operation, he is given preoperative medication and wheeled up to surgery, and then allowed to wait for anywhere from ten to thirty minutes. Dr. Galloway mentioned one phase of this, but I think in addition to having cotton in the ears, the patient should be carefully moved from bed to a cart and taken to surgery without having to sit around in a chair.

Mention has been made of myringotomy. We would all like to have some simple anesthesia for use in children. I have used ether

during the last few years because it seems to have an element of safety, and I think until it has been proved that some other anesthesia is as satisfactory, I shall use ether for this operation.

Dr. Francis Lederer: I should like to voice a word of appreciation of those people who worked in this field long before physicians were sufficiently interested to make of it a science and specialty. Some years ago it was quite impossible to interest hospital and administrative officers in employing men and women physicians who made a specialty of anesthesia. I am sure we have all had the services of excellent nurses who were quite competent, but it has now reached the point where it is actually a science. These people know all about drugs and their reactions, and as a result I feel that a great deal of progress has been made. Much of the credit is due to Dr. Waters of Madison, who has trained many people. We can entrust our patients to the anesthetist and know that anesthesia is properly carried out, thus relieving us of much responsibility. You will all remember how ill at ease you used to feel with premedication and anesthesia, but now you can rest assured that your patient is competently and comfortably taken care of. We should all see to it that our hospitals are properly staffed with members of this specialty. Another point that is not always taken into consideration is the fact that a good anesthetic agent reduces the time of convalescence. A patient who is able to command the services of a good surgeon gives no consideration as to who is going to give him an anesthetic, and I think we, as surgeons, should protect our patients by seeing to it that the anesthetic is administered by a person who is trained in this field.

Dr. Sherman Shapiro: I would like to ask Dr. Cullen his opinion of ethylene as an anesthetic, particularly in the performance of a mastoidectomy.

Dr. George Woodruff: With reference to myringotomy, in my experience nitrous oxide is very satisfactory in the hospital in both children and adults. But in the home we occasionally have a patient whom we cannot take to the hospital, and we do not like to use local anesthesia, which is unsuitable for children and often results in an inadequate incision. We used to use ethyl chloride and, while we have had no unfavorable experiences, I am somewhat afraid of it, having heard so much about the danger. I think it is a problem to know what to use.

Dr. Glenn Greenwood: I would like to ask what the routine medication would be in a patient weighing 150 pounds, who came for diagnostic bronchoscopy.

DR. ROBERT GOOD: I agree with what Dr. Ballenger said about scopolamine. I had a patient in a small hospital who was given barbital two hours prior to operation, then a hypodermic of scopolamine and morphine one-half hour before I performed a submucous resection. He was taken back to bed with the nose packed, and when I got back to his room he was not breathing; had I not arrived when I did he might have died.

Scopolamine should be used cautiously in old people. I had a patient aged 80 who was given scopolamine prior to injection for trifacial neuralgia, and he developed hypostatic pneumonia. I think there is too much relaxation. Dr. Cullen mentioned that it should be used early enough so that the action would not be prolonged. I had hoped he would speak of the topical application of anesthesia on the mucous membrane. I wish someone would report a thorough analysis of the use of cocaine alone and in combination with adrenalin, with a study of the symptoms, and a comparison of patients sitting and in the recumbent position.

I saw in one of the London hospitals some time ago, a boy who was sitting waiting for the doctor, and the nurse said the nose had been packed with cocaine pads but the doctor was late. I am opposed to putting cotton soaked with cocaine into the nose. It is not necessary to have it absorbed into the venous system. A few applications of cocaine and adrenalin chloride with a cotton applicator is sufficient, and avoids excessive absorption.

DR. WALTER THEOBALD: Dr. Cullen represents a new science and art, and hospitals are coming to recognize that they must have a department of anesthesia under the direction of a qualified and experienced anesthetist. I should like to ask whether, in simple operations such as tonsillectomy and adenoidectomy in children, he recommends or uses any premedication, and what his choice of anesthesia would be in such operations.

DR. STUART C. CULLEN (closing): Drs. Ballenger, Galloway and Good have mentioned the advisability of aiding premedication by assuring perfect quiet and rest for the patient preoperatively. I concur heartily with them. The desired mental and metabolic state cannot be obtained merely by giving the right amount of the right drugs at the right time.

In order that there be no misconception, I should like also to emphasize that we do not give large doses of premedicating drugs and then forget the patient. In many cases in which we think the premedication may cause sufficient narcosis to allow the patient to

become obstructed, we give the drug intravenously after we have him under our supervision, so that we may take care of the airway and the oxygen supply.

With reference to the respiratory depressant effect of scopolamine, from Dr. Waters' clinical investigation and our clinical impression from its use in thousands of cases, we would say it is a respiratory stimulant; that is one of the principal reasons for using it in combination with morphine. We have seen but one true scopolamine reaction in several thousand cases.

In answer to Dr. Galloway's question, we find that there is a minimal depression of the cough reflex even with large doses of the combination of barbiturate, morphine and scopolamine. We use that combination of drugs in patients with productive cough undergoing thoracoplastic procedures with nitrous oxide anesthesia and find no appreciable diminution of the cough reflex.

The matter of anesthesia for operations on the head and upper respiratory passages in which the endotherm is to be used is difficult. In order of preference we use local or regional technics, nitrous oxide, pentothal, or chloroform. In each instance, however, a patent airway is established, which in many cases means an endotracheal catheter.

Dr. Weiss inquired concerning the use of various agents in the presence of a high blood sulfanilamide level. Only one agent is contra-indicated, pentothal, and that on the basis of experimental work by Adriani, who demonstrated a marked lowering of the minimum lethal dose of pentothal in rats given sulfanilamide.

The problem of anesthesia in minor surgical procedures in home and office is difficult, and the ideal agent and technic are not yet apparent. Our practice is to use whatever agent or technic seems best suited to the individual child and surgical procedure. In any event, care must be taken to avoid trouble and preparation must be made to remedy trouble as it develops. Many unfortunate deaths in just such cases have occurred because the anesthetist was unprepared for accidents.

My personal feeling about ethylene is that anything that can be done with ethylene can be done with nitrous oxide, and with less danger to the patient.

I am unable to answer Dr. Greenwood's question concerning the dosage of drugs for bronchoscopy in a man weighing 150 pounds.

It is essential that the patient be seen and all factors, particularly the age, be considered in estimating the dosage.

Our usual anesthetic procedure in tonsillectomy is open drop ether. We have minimal difficulty with it and see no particular reason for abandoning it. We see no reason why children should not be premedicated with morphine.

In conclusion, I wish to compliment Dr. Lederer as a pioneer in anesthesia in Chicago. Although he disclaims being an anesthetist, he certainly must have been a good promoter.

CHICAGO LARYNGOLOGICAL AND OTOLOGICAL SOCIETY

Meeting of Monday, January 6, 1941

THE VICE-PRESIDENT, DR. JEROME STRAUSS, IN THE CHAIR

Carcinoma of the Esophagus: Endoscopic Experiences During the Past Year

E. W. HAGENS

(Abstract)

The report covers eight cases of carcinoma of the esophagus seen during the past year, and details of each are given. The essayist stressed the value of endoscopic examination in these cases. It is highly desirable that diagnosis be made early. One of the conditions encountered is the border of firm, fixed edematous tissue lying just proximal to the actual lesion. This tissue is covered by epithelium of normal appearance, and may be of such size that to bite through it would be dangerous. The esophagus is usually narrowed by this tissue so that it is practically impossible to see or get at the tumor itself. A small esophagoscope can be inserted in the large one and through the strictured area, or inserted alone. This, however, narrows the field of vision and necessitates a much smaller biopsy forceps. Also, the narrow area with its rigidity limits the mobility of the esophagoscope considerably. Hence one is often faced with the choice of either making a diagnosis from the local findings or taking a chance of perforating by biting deeply into the tissue for biopsy. Taking the usual bite into the edematous tissue leads to a negative diagnosis for carcinoma.

The endoscopist carries considerable responsibility when it is realized that an early positive diagnosis may make surgery possible, whereas an indeterminate report may cause the thoracic surgeon to fear exploration, and as a result of waiting the case becomes too far advanced for surgery. It is sometimes advisable to take several biopsies, if possible from different sites. Many times re-examination is not possible, and the exact diagnosis rests on the single esophagoscopy and biopsy.

One of the difficulties of esophagoscopy frequently is lack of time for adequate preparation of the case. It is advisable whenever possible for the endoscopist to take a complete history, see the barium fluoroscope and study the pictures, as well as make a complete examination of the patient.

The points brought out by this study serve to emphasize that carcinoma of the esophagus should be borne in mind in all doubtful cases and should be carefully sought for. It is advantageous that the patient be cared for by a group of men who are accustomed to working together, as such groups are more likely to arrive at an early accurate diagnosis and plan more adequate treatment.

DISCUSSION

DR. JOHN R. LINDSAY showed slides of scirrhous and medullary types of esophageal carcinoma.

DR. PAUL HOLLINGER: Dr. Hagens has stressed a number of interesting points. One of his most important statements, I believe, was that in the cases he presented no ill effects resulted from either the direct examination itself or the removal of tissue from the esophagus for biopsy. This emphasizes again the safety of a procedure which is indispensable for making a correct diagnosis.

I should like to stress another point in regard to carcinoma of the esophagus. This concerns the early diagnosis of the disease, prior to X-ray evidence of its presence. Two factors are responsible for negative fluoroscopic and radiographic findings in early esophageal carcinoma. The first is that a carcinoma may be situated on the wall of the thoracic esophagus but not be large enough to give a constant filling defect. The second is that a carcinoma may be situated high in the cervical esophagus at a point where the barium column is forced downward so rapidly by the strong muscles of the hypopharynx that a small, irregular, constant filling defect will be unnoticed. Thus, in a plea for early diagnosis of carcinoma of the esophagus we must stress the importance of esophagoscopy in spite of negative roentgen findings, if symptoms are suspicious of esophageal obstruction. The same holds true of bronchogenic carcinoma, of course, because tumors of the bronchi frequently manifest themselves clinically several months before they are demonstrable roentgenologically.

DR. W. E. ADAMS: It was a pleasure to hear Dr. Hagens' paper and the discussion on this subject, one in which I have been much interested. I think this group is going to play a significant part in the progress of the treatment of these lesions.

To give you some idea of the magnitude of the problem, statistics gathered by Dormanns from 42 German institutions between 1925 and 1933 are as follows: Of 124,827 autopsies on patients with all kinds of malignancies, 23,139 deaths were due to carcinoma of the esophagus, which represents about 8% of all malignant tumors in men over 20 years of age. If one considers 150,000 deaths per annum in the United States due to malignancy, he can get some idea as to the number of deaths each year due to carcinoma of the esophagus.

On being asked to discuss the subject before the American College of Surgeons last October, I corresponded with a number of surgeons interested in carcinoma of the esophagus, and gathered statistics relative to its surgical treatment. Of 67 explorations of carcinoma of the esophagus, there were 34 successfully resected by 12 groups of men in the last two years. Prior to that time there were only 29 successful resections, the first being done by Torek in 1913. Of these 34, 22 were of the Torek type of operation and 12 were of the type where the tumor is resected and the esophagus anastomosed with the stomach. Of these 34 successful resections 20 were living at the time the statistics were gathered, up to as long as four years after operation.

Early diagnosis is essential for successful surgical treatment. If it can be made within a relatively short time after onset of symptoms, say within two or three months, about 40% of the cases will be operable; 60% will have had local extension into adjacent structures or metastases. A high percentage of patients having dysphagia will seek the aid of a throat specialist; thus this group will play an important part in making early diagnoses by endoscopic examinations and biopsy. If the first biopsy reveals no evidence of carcinoma, a second should be made without further delay. This is very important since carcinoma is the cause of dysphagia in a high percentage of cases.

Although definite progress has been recently made in this field, more may be expected when early diagnosis becomes more frequent.

DR. SAMUEL SALINGER: There are two points on which I should like to comment briefly. One is that the scirrhous type of carcinoma is not as rare as one might suppose, since Dr. Hagens has just shown several slides of cases of this type. I can recall having seen only two of these cases over a long period of years, and at the time I was impressed with the fact that they were rather uncommon. In one of these cases it was impossible to obtain a positive biopsy, but at autopsy

we found that the growth had formed an enormous, heavy, constricting ring about the lower end of the esophagus without breaking through the mucous membrane at any point.

The other point is in relation to the use of surgical diathermy as a palliative in the inoperable cases. I employed diathermy in two cases and felt that by destroying the granulomatous masses which were present, I lessened the amount of hemorrhage and also kept the passage open for feeding. Naturally there is some danger of perforation if the treatment is too vigorously applied, and perhaps this is the reason why it is not used more frequently. In another instance the diathermy was applied to the lower end of the esophagus by way of a gastrostomy. I should like to know whether this type of procedure was ever used in any of Dr. Hagens' cases.

DR. E. W. HAGENS (closing): In reply to Dr. Salinger, we have contemplated using diathermy on our cases. I wish to thank the discussors, and I am sure they have added a great deal to the subject.

Factors Influencing the Hearing Improvement After Fenestration for Otosclerosis

GEORGE E. SHAMBAUGH, JR.

(Abstract)

The best reported results with the fenestration operation have followed the use of the one-stage technic of Lempert. The original technic, however, gave results that still left much to be desired. In Lempert's first report, 19 of 23 patients operated upon experienced improvement in hearing, but a report two years later showed that 9 of the 19 were subsequently reoperated upon because they had lost the improvement.

The essayist reviewed his own results from July 1938 to January 1940, during which period the operation was employed in 13 patients, 2 of whom had operations on both ears, making a total of 15 fenestrations in a year and a half. In each case Lempert's technic was followed correctly, and yet the final results were disappointing. Only 3 fenestra remained open with a lasting and significant improvement in hearing.

In January 1940, one fenestra that had closed a year before was revised. On elevating the skin from the horizontal semicircular canal the fistula was found to be completely occluded by a plug of new bone with a granular appearance as though formed from bone

dust. Apparently the removal of bone dust by cotton applicators dipped in saline had not prevented some of the dust from the finishing burr from falling into the fistula. A simple irrigating apparatus was then devised to maintain a constant flow of warm sterile normal saline across the horizontal canal during creation of the fenestra. Not only was every particle of bone dust washed away, but the field was kept perfectly clean and free from blood. This improvement in technic has now been used in 40 new fenestra and 10 revisions, and in not one has complete bony closure of the fenestra occurred.

The final result of the operation was unsatisfactory in 7 out of 40 new fenestra and in 2 of 10 revisions. Seven of the 9 poor results were due to generalized or localized serous labyrinthitis, possibly caused by trauma, infection, or by blood or serum from the under surface of the skin flap. To overcome or minimize postoperative serous labyrinthitis, two further modifications of technic have been devised. Sulfanilamide or sulfathiazole is used in the wound, and the operation is performed under a binocular dissecting microscope. The value of this more meticulous technic will no doubt become evident.

In summarizing the results on a total of 50 patients, 4 of whom had both ears operated on and 11 of whom had revisions, the essayist believes that the refinements of technic have not only improved the proportion of successful cases, but the lasting gain in hearing has greatly increased. There have been no deaths, no serious complications, and no case where the hearing in the ear operated upon has been made worse.

DISCUSSION

DR. WALTER THEOBALD: I would like to ask Dr. Shambaugh whether he has been able to cover the fenestration with the tympanic membranous flap. The distance is so great that I wonder whether there has been some retraction from the fenestration. I am reminded of the radical operation in which an amniotic flap was used. That might be a thought if the tympanic membranous flap were not sufficient.

DR. GLENN GREENWOOD: I wonder whether or not some of the success attributed to the removal of bone dust might accrue from the fact that the temperature due to friction of the burr is here somewhat more controlled. I wish to commend Dr. Shambaugh for adapting this excellent apparatus to this field.

DR. GEORGE SHAMBAUGH (closing): In answer to Dr. Theobald, the tympano-meatal flap is always long enough to reach well

up over the fistula. However, I am certain that Shrapnell's area does not reach the fistula except in exceptional cases. I spend a good deal of time with the binocular magnifying loupe picking off little fragments of bone from the part of the skin flap which will cover the region of the fistula, which means to me that that part of the membrane was not Shrapnell's but was from the bony canal wall. However, in each case the skin is long enough to cover the fistula without trouble.

In answer to Dr. Greenwood, concerning the heat generated by the burr—why the finishing burr seems to inhibit bone regeneration has not been answered as yet. Certainly with irrigation there is no heat generated, and this should help to protect the membranous labyrinth.

Orbital Cellulitis

L. J. WALLNER

(Author's abstract)

Acute sinusitis accounts for 70 to 80% of all cases, the ethmoid more commonly in infants, the frontal in adults. The acute sinusitis of scarlet fever and that following swimming are especially liable to cause orbital involvement.

Several types of pathology have been described as the cause of the symptoms of chemosis, proptosis, fixation, edema and redness of the lids. The same symptoms are present in cavernous sinus thrombosis, due to venous obstruction. It is suggested that venous stasis is the prominent factor in orbital cellulitis, whether due to a subperiosteal abscess, true cellulitis of the orbit or thrombophlebitis. Some experiments were performed on dogs, showing the effect of pressure on the ophthalmic veins, causing proptosis, chemosis and edema of the lids.

Ten cases of orbital cellulitis are listed briefly; two followed scarlet fever; four followed swimming. There were two deaths, and the postmortem findings are described.

Conservative measures are advised: local astringents in the nose, hot applications, X-ray therapy and chemotherapy.

DISCUSSION

DR. ALFRED LEWY: I have seen four cases of orbital cellulitis in adults following inflammation of the antrum. Most cases seen in

children are associated with ethmoid inflammation, as Dr. Wallner said. I have seen only two associated with other sinus inflammations. One of the cases was that of orbital cellulitis associated with scarlet fever, before the days of convalescent serum and sulfathiozol. I recommended operation, which was not done, and the child recovered. Under more conservative treatment I have seen a number of patients recover, two of whom were treated by irrigation of the maxillary sinus. In one case I believe there was a beginning osteomyelitis of the superior maxilla.

DR. HOWARD C. BALLENGER: I believe there is no question but that a few cases of orbital cellulitis are due to infections of the maxillary sinus. However, in my experience, the ethmoid has been a much greater factor.

Several years ago I went over the records of all cases of orbital cellulitis and orbital abscess at the Children's Memorial Hospital. In about 10% of these cases some form of surgical drainage was necessary. The other 90% subsided without surgical intervention. Recently I have had a boy 12 years of age who had an orbital cellulitis without any evident orbital abscess, who recovered with hot compresses and local medication but has been left with limited extraocular motion of the involved eye. It is possible that if some form of surgical drainage had been instituted the loss of eye motion might have been avoided.

The Pathology of Benign Polyps of the Larynx

S. A. FRIEDBERG

(No abstract or paper submitted)

DISCUSSION

DR. WALTER H. SEGAL: One question is, why do polyps develop just on or near the edge of the vocal cord? Polyps develop in the subepithelial space, which surrounds the vocal cord and is limited in all directions. It extends from the anterior commissure to the *processus vocalis*, and above and below about to the border where the stratified epithelium goes into cylindrical epithelium. To demonstrate this space, Hajek injected it with a stained mass, which shows that the subepithelial space is limited outside by the elastic membrane or *ligamentum vocale*. Anteriorly and posteriorly the elastic membrane shades into the cartilage. Above and below the

membrana propria takes on a different texture with many mucous glands in it which are surrounded by elastic fibers, and it is therefore dense and resistant. This is the outer border of the space; the medial border is formed by the stratified epithelium which reaches above and below about 1.5 or 2 mm. from the free edge of the vocal cord. It consists of 10 to 20 layers of stratified epithelium. At the edge and on the upper surface near the edge it is thin and there are only two or three layers. This thin epithelium forms a *punctum minoris resistantiae*, and if there is congestion with secondary edema the thin epithelium at the medial border of the Reinke space gives way. The elastic membrane, interlaced with muscle fibers, offers too much resistance to be affected by the pressure.

The second point is the vascularization of the vocal cord. The arteries are scarce, but the veins are numerous and large and form three separate nets lying one above the other. In the vocal cords this superficial net forms long stretched meshes. Through increased and prolonged pressure these thin and numerous veins can easily become compressed, and congestion may develop in this space.

The last point deals with the question of why polyps usually develop at the border of the anterior and middle third of the vocal cord. The cords work in somewhat the same manner as the lips of a reed pipe, which is blown on from below. The vocal cords move from the middle to the side and back again, and thus develop nodes and antinodes. The nodes are points which are resting, while the bordering parts are in motion. Gutzmann has shown that at the point where polyps develop there is a sort of vibrational node. The vocal cords do not come in contact at this point, while they do so elsewhere. It has also been shown that they are rather concave here. One might speculate from these facts that at the point where the cords are at rest and are concave in shape, blood could accumulate and stasis develop, with consequent edema, thrombosis and hyalinization. Polyps are therefore most frequent in men, and particularly in those who habitually overstrain their voices, as in singers. Rapidly developing polyps are found at the same place as those which are chronic. Often these polyps rupture and heal up without intervention. It may be said, then, that anatomic and functional disorders work together to produce polyps. Changes of inflammatory nature, if present, are secondary and disappear when the polyps have been removed and the functional disturbances have been eliminated.

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